EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	209	@pd>"20060101" and (544/363 or 514/253.06)".ccls"	US-PGPUB; USPAT	OR	OFF	2007/08/19 19:59

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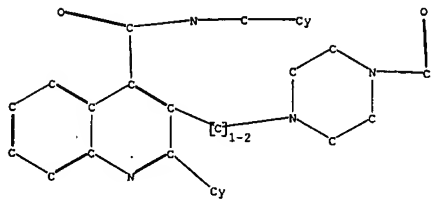

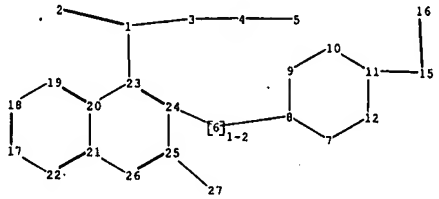

10/561745

chain nodes :
1 2 3 4 5 6 15 16 27
ring nodes :
7 8 9 10 11 12 17 18 19 20 21 22 23 24 25 26
chain bonds :
1-3 1-2 1-23 3-4 4-5 6-8 6-24 11-15 15-16 25-27
ring bonds :
7-8 7-12 8-9 9-10 10-11 11-12 17-18 17-22 18-19 19-20 20-21 20-23 21-22
21-26 23-24 24-25 25-26
exact/norm bonds :
1-3 1-2 3-4 4-5 6-8 7-8 7-12 8-9 9-10 10-11 11-12 11-15 15-16 25-27
exact bonds :
1-23 6-24
normalized bonds :
17-18 17-22 18-19 19-20 20-21 20-23 21-22 21-26 23-24 24-25 25-26

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:Atom 6:CLASS 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom
22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom

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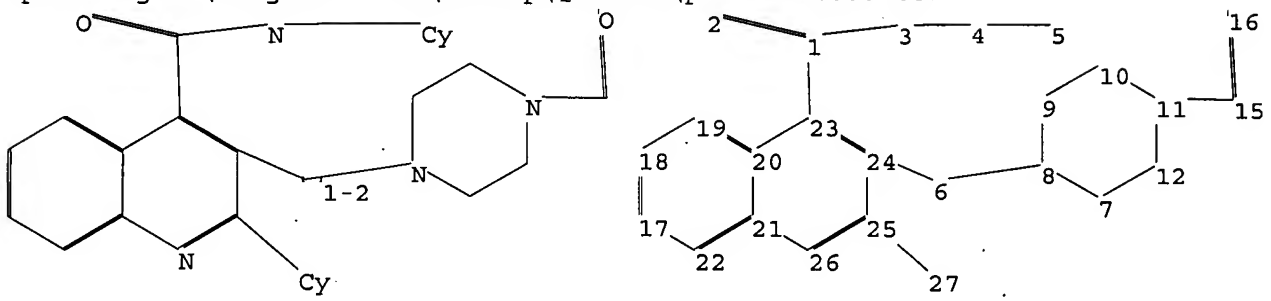

chain nodes :
1 2 3 4 5 6 15 16 27
ring nodes :
7 8 9 10 11 12 17 18 19 20 21 22 23 24 25 26
chain bonds :
1-3 1-2 1-23 3-4 4-5 6-8 6-24 11-15 15-16 25-27
ring bonds :
7-8 7-12 8-9 9-10 10-11 11-12 17-18 17-22 18-19 19-20 20-21 20-23 21-22
21-26 23-24 24-25 25-26
exact/norm bonds :
1-3 1-2 3-4 4-5 6-8 7-8 7-12 8-9 9-10 10-11 11-12 11-15 15-16 25-27
exact bonds :
1-23 6-24
normalized bonds :
17-18 17-22 18-19 19-20 20-21 20-23 21-22 21-26 23-24 24-25 25-26

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:Atom 6:CLASS 7:Atom 8:Atom 9:Atom
10:Atom 11:Atom 12:Atom 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom 20:Atom
21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom

L1 STRUCTURE UPLOADED

=> s l1
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SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 5 TO 234
PROJECTED ANSWERS: 5 TO 234

L2 5 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 16:41:01 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 97 TO ITERATE

100.0% PROCESSED 97 ITERATIONS 84 ANSWERS
SEARCH TIME: 00.00.01

L3 84 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	155.84	156.05

FILE 'CAPLUS' ENTERED AT 16:41:11 ON 05 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 5 Dec 2004 VOL 141 ISS 24
FILE LAST UPDATED: 3 Dec 2004 (20041203/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 8 L3

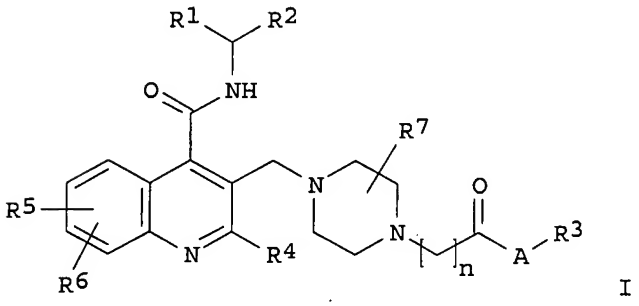
=> d l4 1-8 bib abs hitstr

L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:648345 CAPLUS
DN 141:190803
TI Preparation of quinoline derivatives as NK-2 and NK-3 receptor antagonists
IN Kerns, Jeffrey; Jin, Qi; Wan, Zehong; Nie, Hong; Zhu, Chongjie
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004066950	A2	20040812	WO 2004-US2366	20040129
	WO 2004066950	A3	20041104		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

PRAI US 2003-443650P P 20030130
OS MARPAT 141:190803
GI



I

AB The title compds. [I; R1 = H, (un)substituted alkyl; R2 = (un)substituted aryl, cycloalkyl, heterocyclyl; R3 = H, (un)substituted alkyl, cycloalkyl, aryl, heterocyclyl; A = NR8, O (R8 = H, (un)substituted alkyl); R4 = (un)substituted heterocyclyl; R5 = H, alkyl, alkenyl, aryl, etc.; or R5 represents a bridging moiety which is arranged to bridge two adjacent ring atoms, wherein the bridging moiety comprises alkylene or dioxyalkylene; R6 = H, halo; R7 = oxo; n = 1-4] which are NK2 and NK3 receptor antagonists and are useful in the treatment of respiratory diseases, were prepared E.g., a 4-step synthesis of 3-(4-dimethylcarbamoylmethyl-3-oxopiperazin-1-ylmethyl)-2-(thiophen-2-yl)quinoline-4-carboxylic acid [(S)-1-cyclohexylethyl]amide, was given. The most potent compds. I show IC50 in the range 10-1000 nM against NK-3 receptor binding, and IC50 in the range 1-1000 nM against NK-2 receptor binding. The pharmaceutical composition comprising the compound I is claimed.

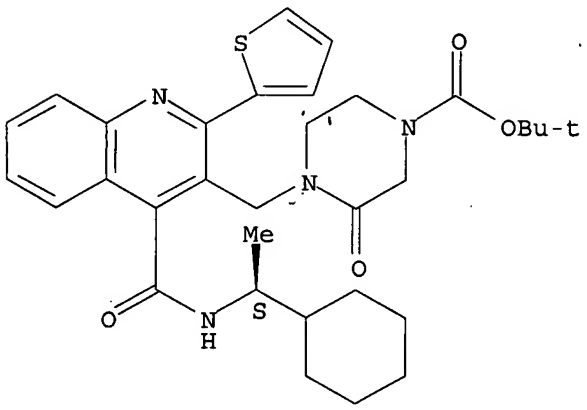
IT **737804-44-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of quinoline derivs. as NK-2 and NK-3 receptor antagonists for treating respiratory diseases)

RN 737804-44-3 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-(2-thienyl)-3-quinolinyl]methyl]-3-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

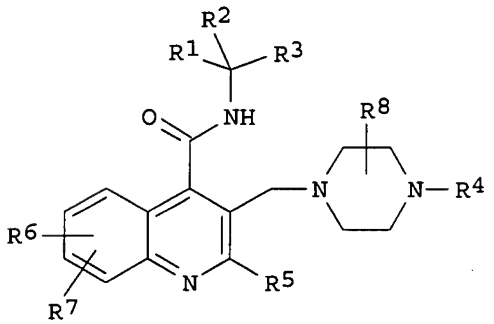
Absolute stereochemistry.



L4 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:814124 CAPLUS
DN 137:337789
TI Preparation of 3-(piperazinylalkyl)-4-quinolinecarboxamide derivatives as NK-3 and NK-2 receptor antagonists for treatment of respiratory diseases and CNS disorders
IN Farina, Carlo; Gagliardi, Stefania; Giardina, Giuseppe Arnaldo Maria; Martinelli, Marisa
PA Glaxosmithkline S.P.A., Italy
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002083664	A1	20021024	WO 2002-EP4070	20020411
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1385839	A1	20040204	EP 2002-761911	20020411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004525184	T2	20040819	JP 2002-581419	20020411
US 2004180902	A1	20040916	US 2004-474557	20040426
PRAI GB 2001-9123	A	20010411		
GB 2002-5649	A	20020311		
WO 2002-EP4070	W	20020411		

OS MARPAT 137:337789
GI



I

AB 3-Substituted quinoline-4-carboxamide derivs. [I; wherein R1 = H, alkyl; R2 = aryl, cycloalkyl, heteroaryl; R3 = H, alkyl, wherein the alkyl group may be optionally substituted by one or more fluorine atoms; R4 = H, hydroxyalkyl, dihydroxyalkyl, hydroxyalkoxyalkyl; R5 = branched or linear

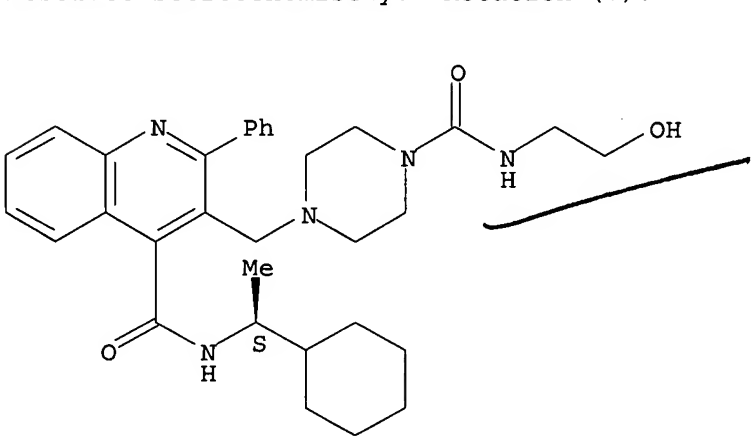
alkyl, cycloalkyl, cycloalkylalkyl, aryl, single or fused ring aromatic heterocyclic group; R6 = H, alkyl, alkenyl, aryl, alkoxy, hydroxy, halo, nitro, cyano, carboxy, carboxamido, sulfonamido, trifluoromethyl, amino, mono- or di-alkylamino; R7 = H, halo; R8 = H, O] were prepared For example, 3-[4-(2-hydroxyethyl)-3-oxopiperazin-1-ylmethyl]-2-thiophen-2-ylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide was prepared by a multistep procedure. The prepared compds. were useful as nk-2 and nk-3 receptor antagonists.

IT **473298-89-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

RN 473298-89-4 CAPLUS

CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-[[(2-hydroxyethyl)amino]carbonyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

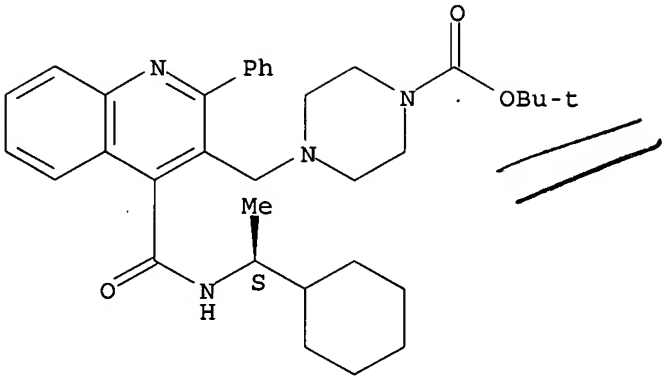


IT **425622-17-9P 473552-94-2P 473553-02-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

RN 425622-17-9 CAPLUS

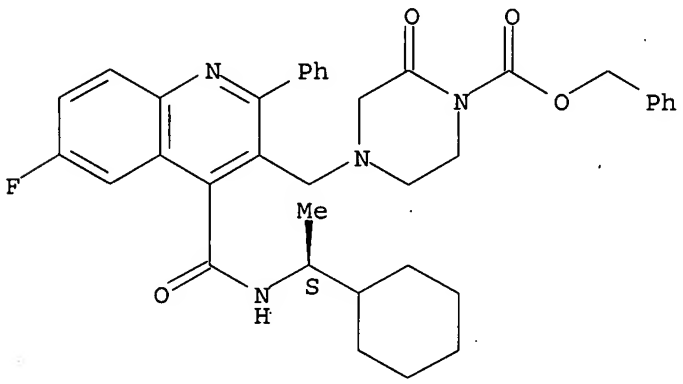
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



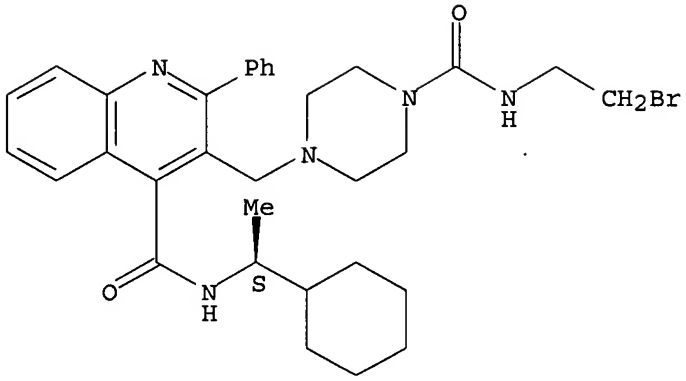
RN 473552-94-2 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-6-fluoro-2-phenyl-3-quinolinyl]methyl]-2-oxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 473553-02-5 CAPLUS
CN 4-Quinolinecarboxamide, 3-[[4-[[(2-bromoethyl)amino]carbonyl]-1-piperazinyl]methyl]-N-[(1S)-1-cyclohexylethyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

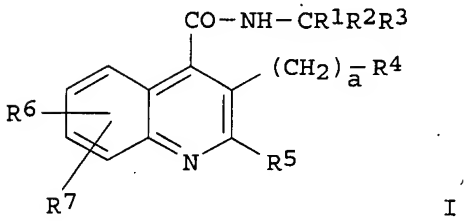


RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:814123 CAPLUS
DN 137:310827
TI Preparation of quinoline-4-carboxamide derivatives as NK3 and NK2 receptor antagonists
IN Farina, Carlo; Gagliardi, Stefania; Giardina, Giuseppe Arnaldo Maria; Martinelli, Marisa
PA Glaxosmithkline S.P.A., Italy
SO PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002083663	A1	20021024	WO 2002-EP4066	20020411
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1377567	A1	20040107	EP 2002-735247	20020411
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004525183	T2	20040819	JP 2002-581418	20020411
	US 2004152726	A1	20040805	US 2004-474542	20040315
PRAI	GB 2001-9123	A	20010411		
	GB 2002-5649	A	20020311		
	WO 2002-EP4066	W	20020411		

OS MARPAT 137:310827
GI



I

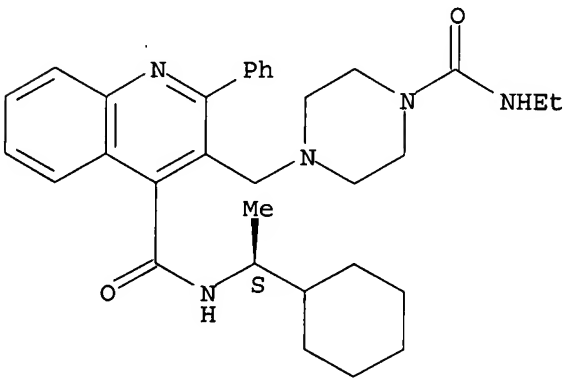
AB Disclosed are quinoline-4-carboxamide derivs. (shown as I; e.g. 6-fluoro-3-[3-oxo-4-(2-piperidin-1-ylethyl)piperazin-1-ylmethyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide), far more stable from a metabolic point of view than the known peptidic NK3 receptor antagonists, as detailed in the specification or a pharmaceutically acceptable salt or solvate thereof, a process for preparing such compds., a pharmaceutical composition comprising such compds. and the use of such compds. in medicine. In I: R1 is H or alkyl; R2 is aryl or cycloalkyl or heteroaryl; R3 is H or alkyl, wherein the group may be optionally

substituted by ≥1 F atoms; R4 is NR8R9; R8 is H, alkyl or R11R12 and R9 is H, alkyl or R13R14; or R8 and R9 together with the N atom to which they are attached form a heterocyclic ring comprising 4-8 ring members, said ring members optionally including in addition to said N atom ≥1 further heteroatoms selected from N, O or S; and further detailed in the specification. Binding assays allowing the determination of the concentration of the individual compound required to reduce by 50% the [125I]-[Me-Phe7]-NKB and [3H]-Senktide specific binding to NK3 receptor in equilibrium conditions (IC50) show the most potent I have IC50 values of 0.1-1000 nM. Binding assays allowing the determination of the concentration of the individual compound required to reduce by 50% the [125I]-NKA and [3H]-NKA specific binding to NK2 receptor in equilibrium conditions (IC50) show the most potent I to have IC50 values of 0.5-1000 nM, such as 1-1000 nM. Example prepns. of about 16 intermediates and 35 I are included.

IT **473298-58-7P**, 3-[(4-Ethylcarbamoylpiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide
473298-59-8P, 3-[(4-Isopropylcarbamoylpiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid ((S)-1-cyclohexylethyl)amide
473298-89-4P, N-((S)-1-Cyclohexylethyl)-3-((4-(((2-hydroxyethyl)amino)carbonyl)-1-piperazino)methyl)-2-phenylquinoline-4-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinoline-4-carboxamide derivs. as NK3 and NK2 receptor antagonists)

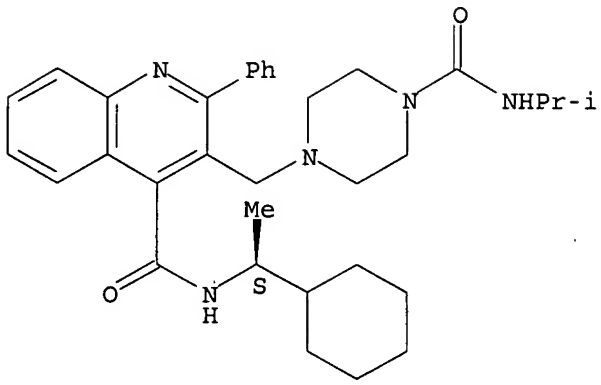
RN 473298-58-7 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-[(ethylamino)carbonyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



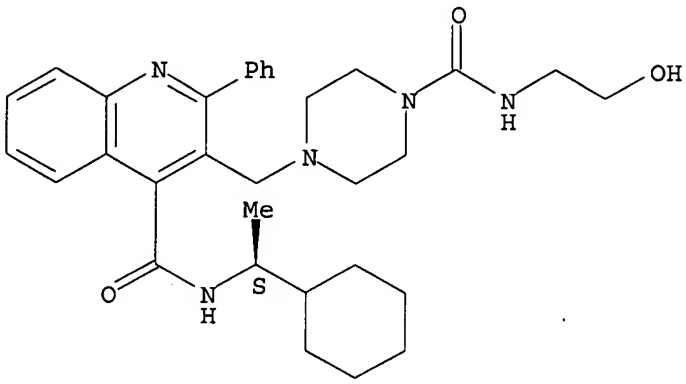
RN 473298-59-8 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-[[(1-methylethyl)amino]carbonyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



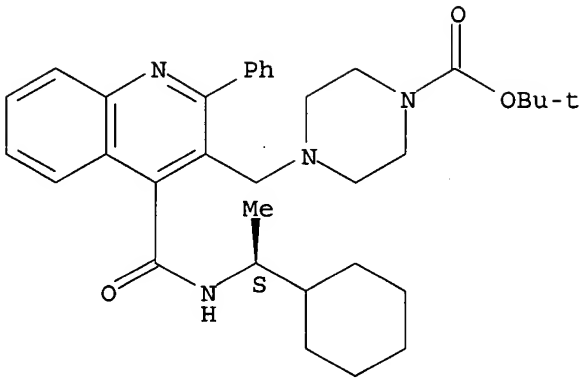
RN 473298-89-4 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-[[(2-hydroxyethyl)amino]carbonyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



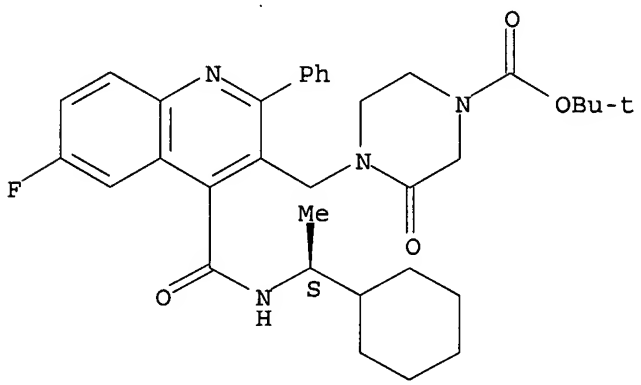
IT **425622-17-9P**, 4-[[4-((S)-1-Cyclohexylethylcarbamoyl)-2-phenylquinolin-3-yl]methyl]piperazine-1-carboxylic acid tert-butyl ester
473298-41-8P, 4-[[4-((S)-1-Cyclohexylethylcarbamoyl)-6-fluoro-2-phenylquinolin-3-yl]methyl]-3-oxopiperazine-1-carboxylic acid tert-butyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinoline-4-carboxamide derivs. as NK3 and NK2 receptor antagonists)
RN 425622-17-9 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 473298-41-8 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-6-fluoro-2-phenyl-3-quinolinyl]methyl]-3-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

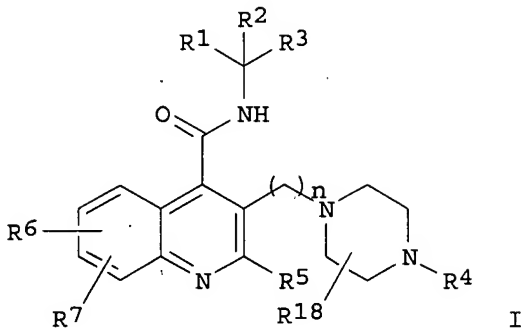


RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:428893 CAPLUS
DN 137:20387
TI Preparation of 3-(piperazinylalkyl)-4-quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders
IN Farina, Carlo; Gagliardi, Stefania; Giardina, Giuseppe; Grugni, Mario; Nadler, Guy Marguerite Marie Gerard; Martinelli, Marisa
PA Glaxosmithkline S.P.A., Italy; Laboratoire Glaxosmithkline S.A.S.
SO PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002044165	A1	20020606	WO 2001-EP13833	20011126
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002026356	A5	20020611	AU 2002-26356	20011126
	EP 1351953	A1	20031015	EP 2001-995670	20011126
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004517082	T2	20040610	JP 2002-546535	20011126
	US 2004097518 SAW	A1	20040520	US 2003-432925	20031124
PRAI	GB 2000-28965	A	20001128		
	GB 2001-9118	A	20010411		
	WO 2001-EP13833	W	20011126		

OS MARPAT 137:20387
GI



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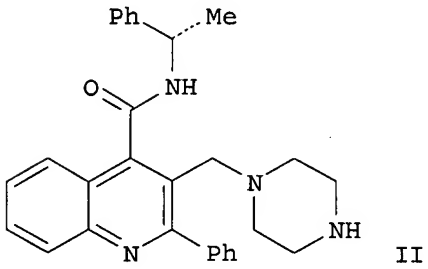


II

AB Title compds. I [wherein R1 = H or alkyl; R2 = (un)substituted (hetero)aryl or cycloalkyl; R3 = H, alkyl, or cycloalkyl(alkyl) (un)substituted by 1 or more fluorines; R4 = H or R8R9; R5 = branched or linear alkyl, cycloalkyl(alkyl), aryl, or single or fused-ring aromatic (un)substituted heterocyclic group; R6 = H, or 1-3 of alkyl, alkenyl, aryl, alkoxy, OH, halo, NO2, cyano, CO2H, alkylcarboxy(alkyl), haloalkyl, NH2, or (di)(alkyl)amino; or R6 = a bridging alkyl or dioxyalkylene; R7 = H or halo; R8 = (un)substituted alkyl or alkenyl; R9 = S(O2)R10, S(O2)OR10, ONO, CO2R10, CONR11R12, or CN; R10 = H, (cyclo)alkyl, or aryl; R11 and R12 = independently H or alkyl; R18 = H or up to 3 oxo groups; any of R2, R5, R8, R10, R11, or R12 may be (un)substituted 1 or more times by halo, OH, NH2, cyano, NO2, CO2H, or oxo; n = 1-6; with 26 compds. excluded; and their pharmaceutically acceptable salts or hydrates] were prepared I are a novel class of potent non-peptide neurokinin-3 (NK-3) antagonists, some of which fall within the generic scope of WO 00/31037. I are far more stable metabolically and show improved oral bioavailability compared to the known peptidic NK-3 receptor antagonists (no data). In addition, I have good NK-2 antagonist activity and are considered to be of potential use in the prevention and treatment of a wide variety of clin. conditions which are characterized by over-stimulation of tachykinin receptors, in particular NK-3 and NK-2. Forty-eight specific (S)-isomeric compds. I were prepared For instance, 4-carboxy-3-methyl-2-phenylquinoline was subjected to the sequence of (1) Me esterification; (2) α-bromination; (3) amination of the bromide with piperazine-1-carboxylic acid tert-Bu ester; (4) ester hydrolysis (95%); and (5) amidation with (S)-1-phenylethylamine to give the title compound II. In binding assays using human NK-2 receptors and guinea pig and human NK-3 receptors, the most potent I exhibited IC50 values ranging from 0.5 nM to 1000 nM and from 0.1 nM to 1000 nM, resp.

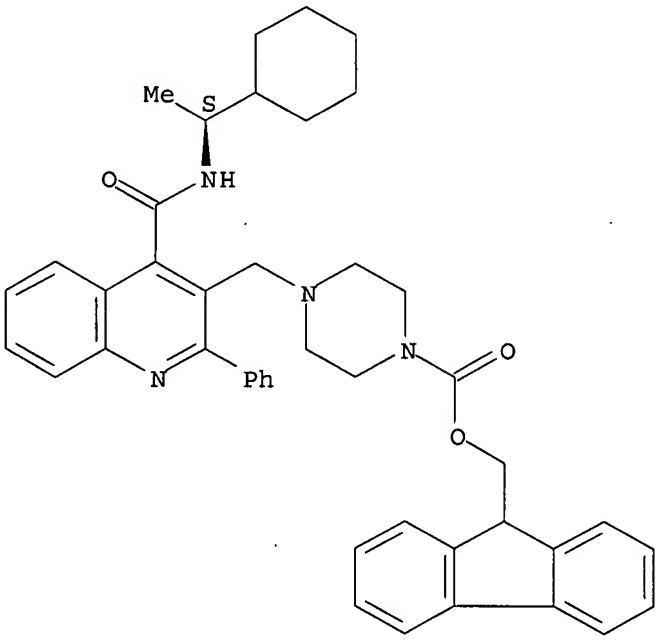
IT **270574-13-5P 270574-14-6P 425622-12-4P 433962-70-0P 433962-95-9P 433962-99-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)

RN 270574-13-5 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

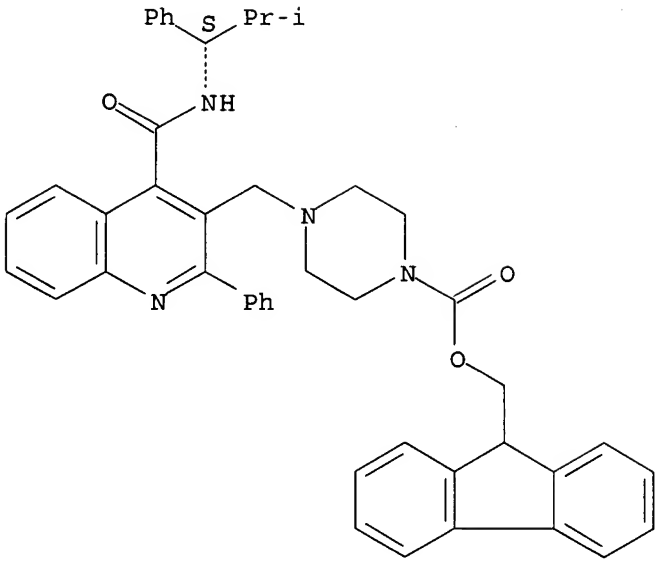
Absolute stereochemistry.



RN 270574-14-6 CAPLUS

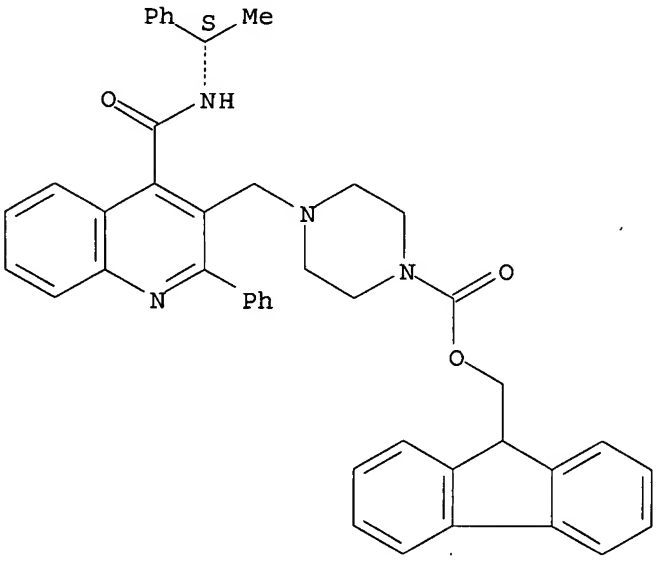
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-2-methyl-1-phenylpropyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



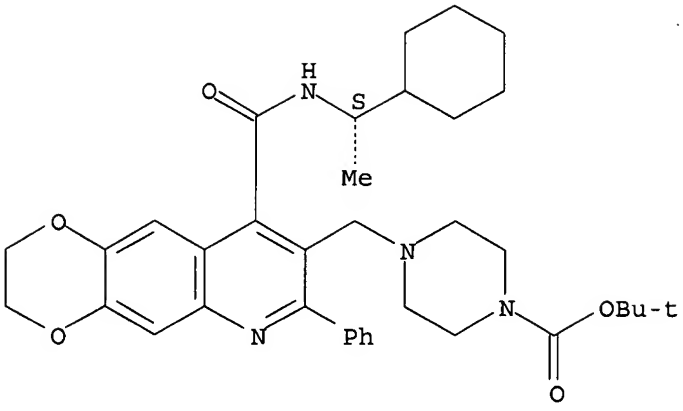
RN 425622-12-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[2-phenyl-4-[[[(1S)-1-phenylethyl]amino]carbonyl]-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



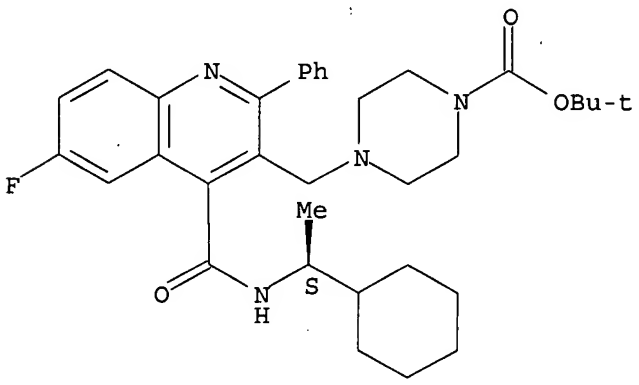
RN 433962-70-0 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[9-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2,3-dihydro-7-phenyl-1,4-dioxino[2,3-g]quinolin-8-yl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



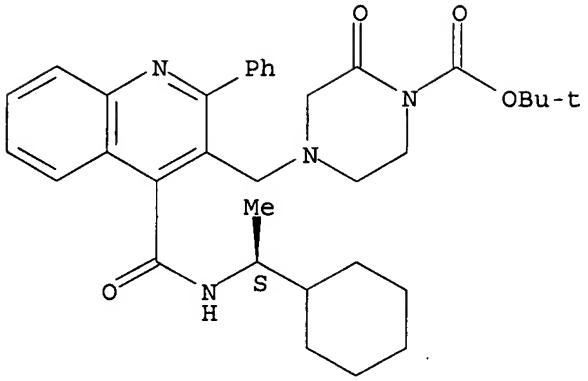
RN 433962-95-9 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbony l]-6-fluoro-2-phenyl-3-quinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



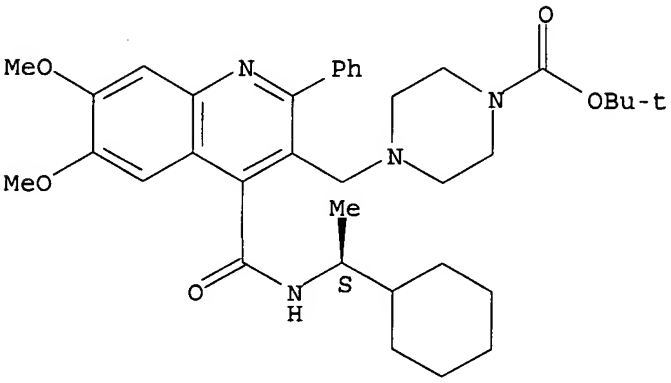
RN 433962-99-3 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbony l]-2-phenyl-3-quinolinyl]methyl]-2-oxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **433963-10-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of piperazinylalkyl quinolinecarboxamides as NK-3 and NK-2 antagonists for treatment of respiratory diseases and CNS disorders)
RN 433963-10-1 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-6,7-dimethoxy-2-phenyl-3-quinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

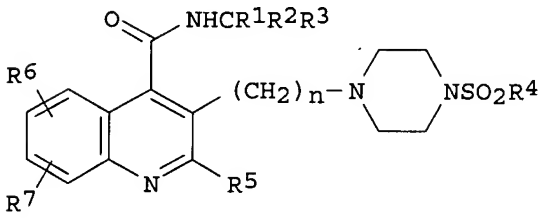


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:368457 CAPLUS
DN 136:369740
TI Preparation of piperazinylalkylquinoline-4-carboxamides as NK-3 and NK-2 receptor antagonists
IN Farina, Carlo; Giardina, Giuseppe; Grugni, Mario; Nadler, Guy Marguerite Marie Gerard
PA Glaxosmithkline S.p.A., Italy; Laboratoire Glaxosmithkline S.A.S.
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002038548	A1	20020516	WO 2001-EP13141	20011112
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002015043	A5	20020521	AU 2002-15043	20011112
	EP 1334088	A1	20030813	EP 2001-983584	20011112
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004513165	T2	20040430	JP 2002-541084	20011112
	US 2004077658	A1	20040422	US 2003-416600	20031023
PRAI	GB 2000-27701	A	20001113		
	WO 2001-EP13141	W	20011112		

OS MARPAT 136:369740
GI



I

AB Title compds. [I; R1 = H , alkyl; R2 = aryl, cycloalkyl, heteroaryl; R3 = H, alkyl, optionally substituted by ≥1 F; R4 = R8R9; R8 = bond, alkyl, aryl; R9 = H, COO R10, NR11R12; R10 = H, alkyl; R11, R12 = H, alkyl; R5 = alkyl, cycloalkyl, cycloalkylalkyl, aryl, single or fused ring heteroaryl; R6 = H, alkyl, alkenyl, aryl, alkoxy, OH, halo, NO2, cyano, carboxy, carboxamido, sulfonamido, alkoxycarbonyl, CF3, acyloxy, amino; R7 = H, halo; n = 1-6; any of R2, R5, R8, R10, R11, R12 may be substituted by halo, hydroxy, amino, cyano, NO2, CO2H, oxo], were prepared Thus, 2-phenyl-3-piperazin-1-ylmethylquinoline-4-carboxylic acid ((S)-2-methyl-1-phenylpropyl)amide (preparation given) in MeCN was treated with

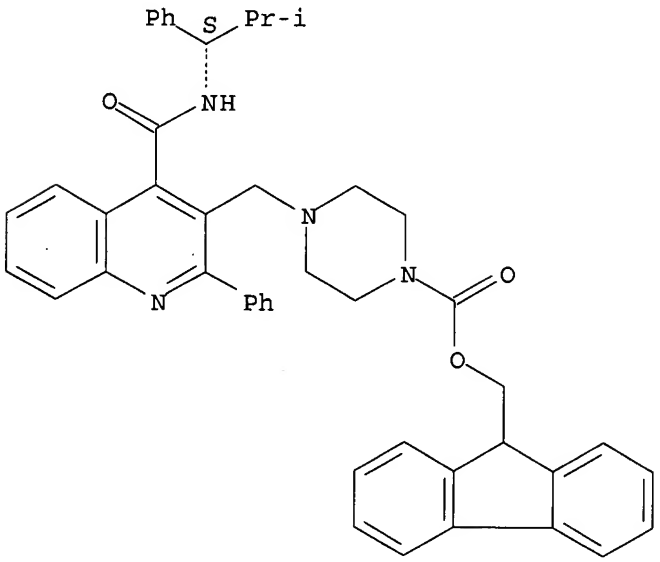
EtO2CCH2CH2SO2Cl and diisopropylethylamine; the mixture was stirred 15 h at room temperature and for 3 h at 50° to give 3-[4-[4-((S)-2-methyl-1-phenylpropylcarbamoyl)-2-phenylquinolin-3-ylmethyl]piperazine-1-sulfonyl]propionic acid Me ester. The most potent I bind to NK-2 receptors with IC50 = 0.5-1000 nM.

IT **270574-14-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of)

RN 270574-14-6 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-2-methyl-1-phenylpropyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

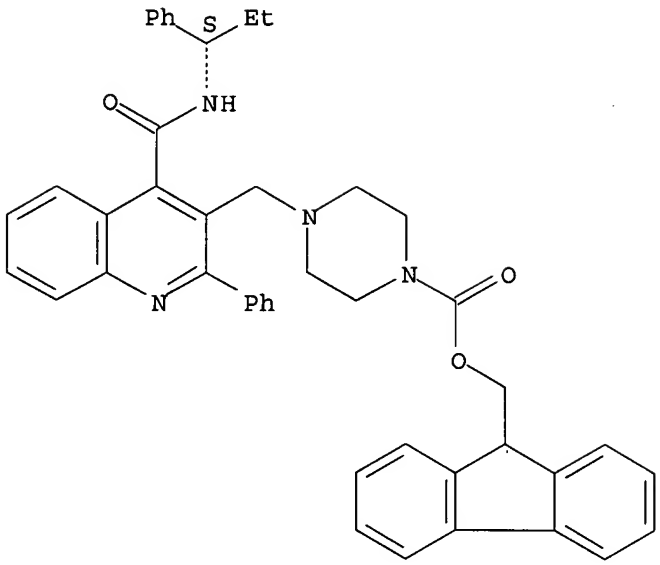


IT **270574-12-4P 270574-13-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazinylalkylquinoline-4-carboxamides as NK-3 and NK-2 receptor antagonists)

RN 270574-12-4 CAPLUS

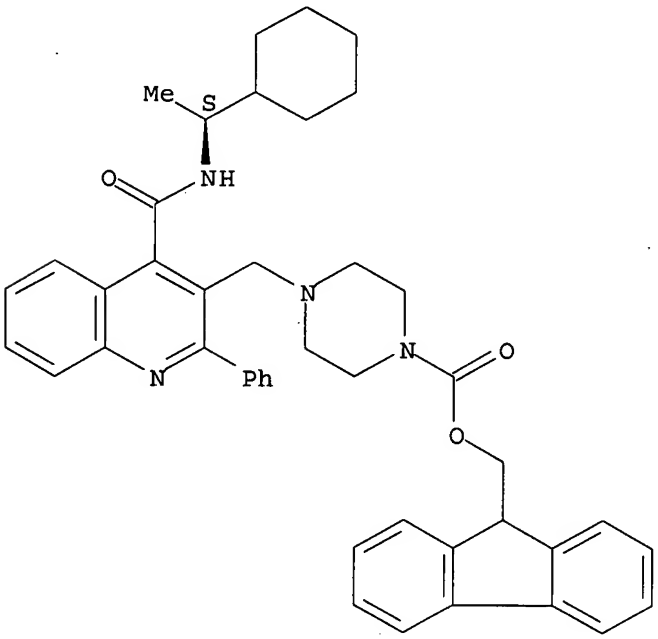
CN 1-Piperazinecarboxylic acid, 4-[[2-phenyl-4-[[[(1S)-1-phenylpropyl]amino]carbonyl]-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 270574-13-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:368456 CAPLUS
DN 136:386030
TI Quinoline derivatives as NK-3 and NK-2 antagonists
IN Farina, Carlo; Gagliardi, Stefania; Giardina, Giuseppe; Grugni, Mario; Martinelli, Marisa; Nadler, Guy Marguerite Marie Gerard
PA Glaxosmithkline S.p.A., Italy; Laboratoire Glaxosmithkline
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002038547	A1	20020516	WO 2001-EP13139	20011112
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002020702	A5	20020521	AU 2002-20702	20011112
	EP 1334089	A1	20030813	EP 2001-993602	20011112
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004517062	T2	20040610	JP 2002-541083	20011112
	US 2004082589	A1	20040429	US 2003-416596	20031023
PRAI	GB 2000-27696	A	20001113		
	GB 2001-9119	A	20010411		
	WO 2001-EP13139	W	20011112		

OS MARPAT 136:386030
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I and their pharmaceutically acceptable salts or hydrates are claimed [wherein: R1 = H or alkyl; R2 = aryl, cycloalkyl, or heteroaryl; R3 = H or C1-3 alkyl, (un)substituted by 1 or more fluorines; R4 = H, R8NR9R10, R11R13, or R11R12R13; R5 = branched or linear alkyl, cycloalkyl(alkyl), aryl(alkyl), or single or fused-ring aromatic heterocyclic group; R6 = H, or 1-3 of alkyl, alkenyl, aryl, alkoxy, OH, halo, NO2, cyano, CO2H, carboxamido, sulfonamido, alkoxycarbonyl, CF3, acyloxy, (di)(alkyl)amino; R7 = H, halo; n = 1-6; R8 = bond or alkylene; R9, R10 = H, alkyl, cycloalkyl(alkyl), aryl(alkyl); or NR9R10 = (un)saturated (fluoro)heterocyclyl; R11 = alkyl, alkenyl, (hetero)aryl, (un)saturated carbocyclyl with ≥1 N/O/S atom(s), cycloalkyl, etc.; R12 = (un)substituted alkyl, alkoxy; R13 = H, CO2R14; R14 = H, alkyl; any of R2, R5, R8, R9, R10, R11, R12, and R14 may be substituted by halo, OH, amino, cyano, NO2, CO2H, or oxo; with specific exclusion of 14 compds.]. Also claimed is a process for preparing the compds., pharmaceutical compns. comprising them, and their use in medicine. I are a novel class of potent non-peptide NK-3 antagonists, some of which fall within the generic scope of WO 00/31037. I are also far more stable from a metabolic point of view than the known peptidic NK-3 receptor antagonists (no data), and are of

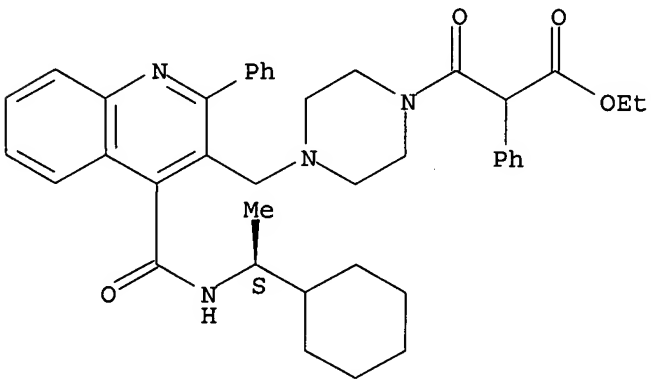
potential therapeutic utility. I also have good NK-2 antagonist activity, and are therefore considered to be of potential use in the prevention and treatment of a wide variety of clin. conditions which are characterized by overstimulation of tachykinin receptors, in particular NK-3 and NK-2. I also show improved oral bioavailability (no data). Approx. 25 specific (S)-isomeric compds. I were prepared, and their general stereochem. forms are claimed. For instance, 3-methyl-2-phenylquinoline-4-carboxylic acid was subjected to a sequence of: (1) Me esterification; (2) α-bromination; (3) amination of the bromide with Fmoc-piperazine; (4) ester hydrolysis; (5) amidation with (S)-1-phenylpropylamine; (6) deprotection at Fmoc; (7) coupling with N-BOC-β-alanine; and (8) deprotection at BOC; to give title compound II, isolated as the di-HCl salt. In binding assays using human and guinea pig NK-3 receptors, and human NK-2 receptors, the most potent I had IC50 values in the range of 0.1-1000 nM for NK-3, and 0.5-1000 nM for NK-2. Antagonist behavior of I at NK-3 receptors was evidenced by reversal of the effects of senktide and NKB, and antagonist activity at NK-2 receptors was indicated by reversal of the effects of NKA.

IT **425621-77-8P**, 3-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-3-oxo-2-phenylpropionic acid ethyl ester
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of quinoline derivs. as NK-3 and NK-2 antagonists)

RN 425621-77-8 CAPLUS

CN 1-Piperazinepropanoic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-β-oxo-α-phenyl-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



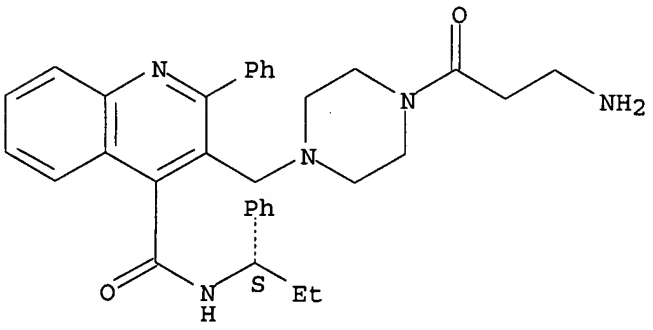
IT **425621-62-1P**, (-)-(S)-N-(1-Phenylpropyl)-3-[[4-(3-aminopropionyl)piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxamide dihydrochloride **425621-63-2P**, 3-[1-[4-[[2-Phenyl-4-[((S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]pyrazine-2-carboxylic acid **425621-64-3P**, 4-[1-[4-[[2-Phenyl-4-[((S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]nicotinic acid **425621-65-4P**, [2-Oxo-2-[4-[[2-phenyl-4-[((S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]ethoxy]acetic acid **425621-66-5P**, [1-[2-Oxo-2-[4-[[2-phenyl-4-[((S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]ethyl]cyclopentyl]acetic acid

425621-67-6P, 3,3-Dimethyl-5-oxo-5-[4-[[2-phenyl-4-[((S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]pentanoic acid **425621-68-7P 425621-69-8P 425621-70-1P**, (E)-4-Oxo-4-[4-[[2-phenyl-4-[((S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]but-2-enoic acid **425621-71-2P**, 3-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-3-oxopropionic acid **425621-72-3P**, 5-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-5-oxopentanoic acid **425621-73-4P**, 3-[1-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]pyrazine-2-carboxylic acid **425621-74-5P**, 3-[1-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]benzoic acid **425621-75-6P**, 5-[1-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]nicotinic acid **425621-76-7P**, 4-[1-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]benzoic acid **425621-78-9P**, 3-[4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-3-oxo-2-phenylpropionic acid sodium salt **425621-79-0P**, 3-[(4-Formylpiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-cyclohexylethylamide **425621-80-3P**, (S)-N-(1-Cyclohexylethyl)-2-phenyl-3-[[4-(phenylcarbamoyl)piperazin-1-yl]methyl]quinoline-4-carboxamide **425621-81-4P**, (S)-N-(1-Cyclohexylethyl)-2-phenyl-3-[(4-carbamoylpiperazin-1-yl)methyl]quinoline-4-carboxamide **425621-82-5P**, 3-[[4-(3-Aminopropanoyl)piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-cyclohexylethylamide **425621-83-6P**, 3-[[4-[3-(Ethylamino)propanoyl]piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-cyclohexylethylamide **425621-84-7P**, 2-Phenyl-3-[[4-[3-(pyrrolidin-1-yl)propanoyl]piperazin-1-yl]methyl]quinoline-4-carboxylic acid (S)-1-cyclohexylethylamide **425621-85-8P**, 2-Phenyl-3-[[4-[3-(piperidin-1-yl)propanoyl]piperazin-1-yl]methyl]quinoline-4-carboxylic acid (S)-1-cyclohexylethylamide **425621-86-9P**, N-(1-Phenylpropyl)-3-[[4-(3-aminopropionyl)piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxamide **425621-87-0P**, 3-[1-[4-[[2-Phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]pyrazine-2-carboxylic acid **425621-88-1P**, 4-[1-[4-[[2-Phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]nicotinic acid **425621-89-2P**, [2-Oxo-2-[4-[[2-phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]ethoxy]acetic acid **425621-90-5P**, [1-[2-Oxo-2-[4-[[2-phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]ethyl]cyclopentyl]acetic acid **425621-91-6P**, 3,3-Dimethyl-5-oxo-5-[4-[[2-phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]pentanoic acid **425621-92-7P**, 2-[1-[4-[[2-Phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]cyclopropanecarboxylic acid **425621-93-8P**, 2-[1-[4-[[2-Phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]cyclohexanecarboxylic acid **425621-94-9P**, 4-Oxo-4-[4-[[2-phenyl-4-[(1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]but-2-enoic acid **425621-95-0P**, 3-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-3-oxopropionic acid **425621-96-1P**, 5-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-5-oxopentanoic acid **425621-97-2P**, 3-[1-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]pyrazine-2-carboxylic acid **425621-98-3P**, 3-[1-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-

phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]benzoic acid **425621-99-4P**, 5-[1-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]nicotinic acid **425622-00-0P**, 4-[1-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]methanoyl]benzoic acid **425622-01-1P**, 3-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-3-oxo-2-phenylpropionic acid ethyl ester **425622-02-2P**, 3-[4-[[4-[(1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazin-1-yl]-3-oxo-2-phenylpropionic acid **425622-03-3P**, 3-[(4-Formylpiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid (1-cyclohexylethyl)amide **425622-04-4P**, N-(1-Cyclohexylethyl)-2-phenyl-3-[[4-(phenylcarbamoyl)piperazin-1-yl]methyl]quinoline-4-carboxamide **425622-05-5P**, N-(1-Cyclohexylethyl)-2-phenyl-3-[(4-carbamoylpiperazin-1-yl)methyl]quinoline-4-carboxamide **425622-06-6P**, 3-[[4-(3-Aminopropanoyl)piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid (1-cyclohexylethyl)amide **425622-07-7P**, 3-[[4-[3-(Ethylamino)propanoyl]piperazin-1-yl]methyl]-2-phenylquinoline-4-carboxylic acid (1-cyclohexylethyl)amide **425622-08-8P**, 2-Phenyl-3-[[4-[3-(pyrrolidin-1-yl)propanoyl]piperazin-1-yl]methyl]quinoline-4-carboxylic acid 1-cyclohexylethylamide **425622-09-9P**, 2-Phenyl-3-[[4-[3-(piperidin-1-yl)propanoyl]piperazin-1-yl]methyl]quinoline-4-carboxylic acid (1-cyclohexylethyl)amide **425622-10-2P**, 3-[1-[4-[[2-Phenyl-4-[(S)-1-phenylethyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]methanoyl]isonicotinic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of quinoline derivs. as NK-3 and NK-2 antagonists)

RN 425621-62-1 CAPLUS
CN 4-Quinolinecarboxamide, 3-[[4-(3-amino-1-oxopropyl)-1-piperazinyl]methyl]-2-phenyl-N-[(1S)-1-phenylpropyl]-, dihydrochloride (9CI) (CA INDEX NAME)

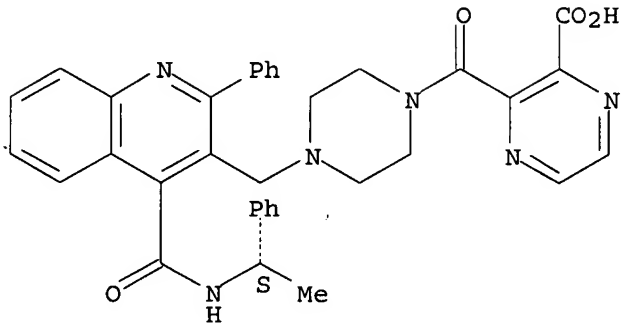
Absolute stereochemistry. Rotation (-).



●2 HCl

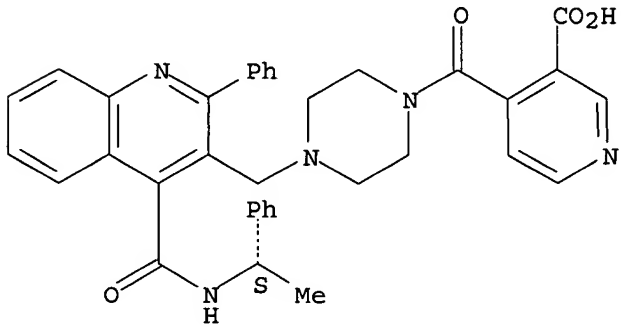
RN 425621-63-2 CAPLUS
CN Pyrazinecarboxylic acid, 3-[[4-[[2-phenyl-4-[[[(1S)-1-phenylethyl]amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



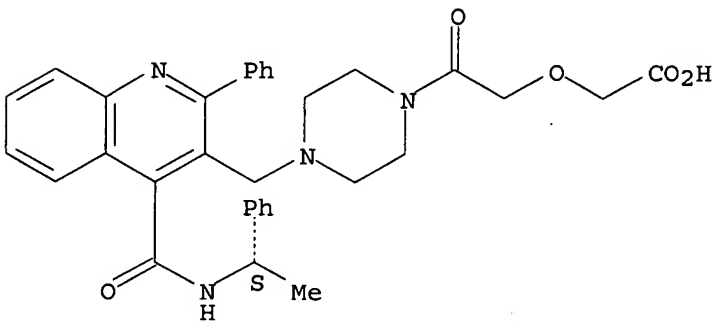
RN 425621-64-3 CAPLUS
CN 3-Pyridinecarboxylic acid, 4-[[4-[[2-phenyl-4-[[[(1S)-1-phenylethyl]amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 425621-65-4 CAPLUS
CN Acetic acid, [2-oxo-2-[4-[[2-phenyl-4-[[[(1S)-1-phenylethyl]amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]ethoxy]- (9CI) (CA INDEX NAME)

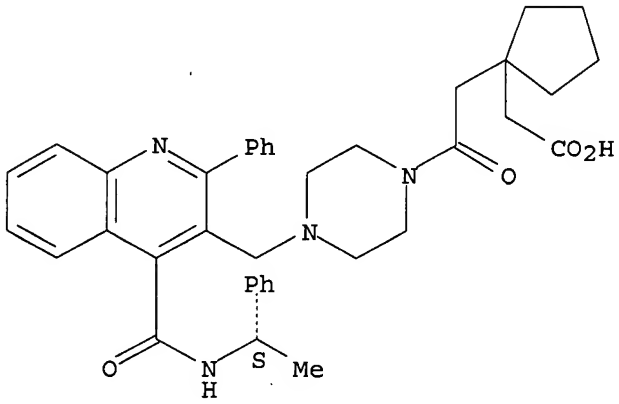
Absolute stereochemistry.



RN 425621-66-5 CAPLUS
CN Cyclopentaneacetic acid, 1-[2-oxo-2-[4-[[2-phenyl-4-[[[(1S)-1-

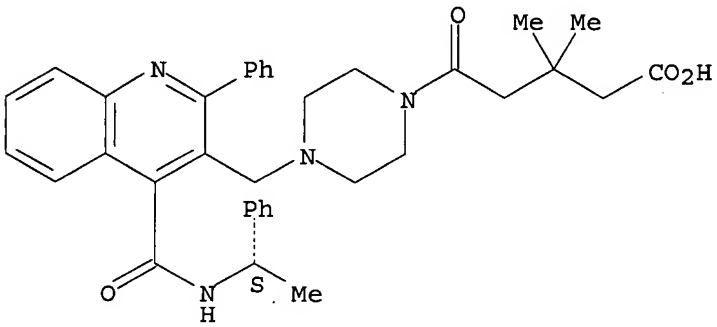
phenylethyl]amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



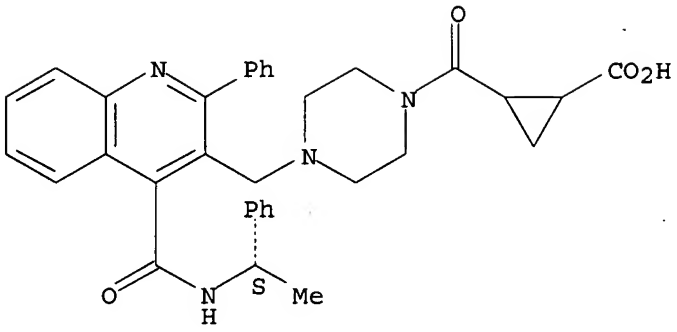
RN 425621-67-6 CAPLUS
CN 1-Piperazinepentanoic acid, β,β-dimethyl-δ-oxo-4-[[2-phenyl-4-[[[(1S)-1-phenylethyl]amino]carbonyl]-3-quinolinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



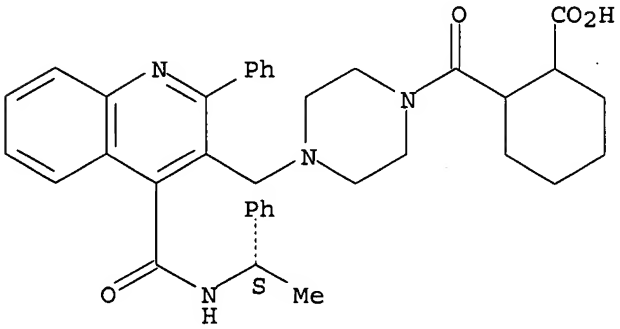
RN 425621-68-7 CAPLUS
CN Cyclopropanecarboxylic acid, 2-[[4-[[2-phenyl-4-[[[(1S)-1-phenylethyl]amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



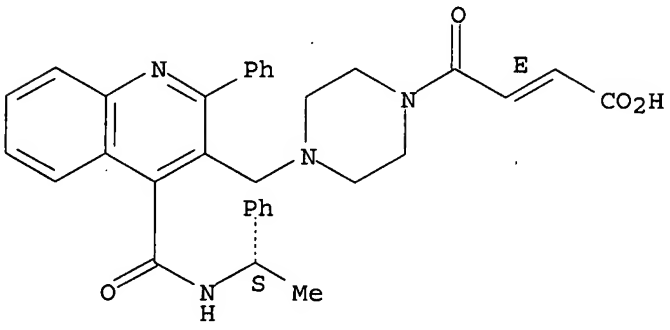
RN 425621-69-8 CAPLUS
CN Cyclohexanecarboxylic acid, 2-[[4-[[2-phenyl-4-[[[(1S)-1-phenylethyl]amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 425621-70-1 CAPLUS
CN 2-Butenoic acid, 4-oxo-4-[4-[[2-phenyl-4-[[[(1S)-1-phenylethyl]amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]-, (2E)-(9CI) (CA INDEX NAME)

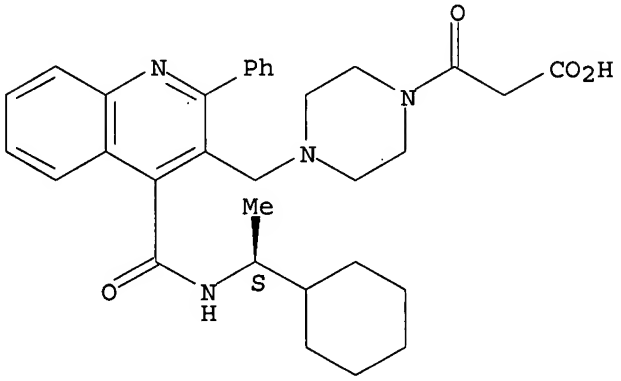
Absolute stereochemistry.
Double bond geometry as shown.



RN 425621-71-2 CAPLUS
CN 1-Piperazinepropanoic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl

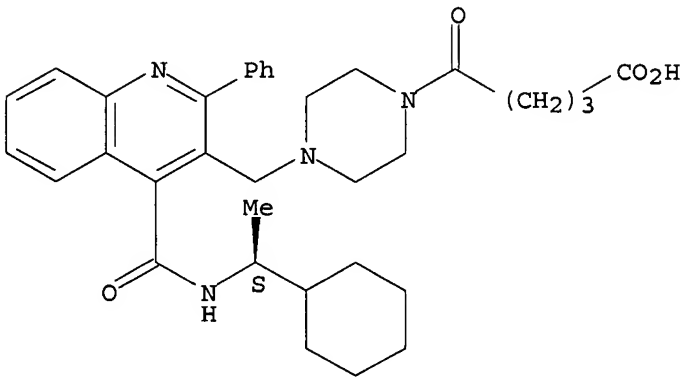
]-2-phenyl-3-quinolinyl]methyl]-β-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



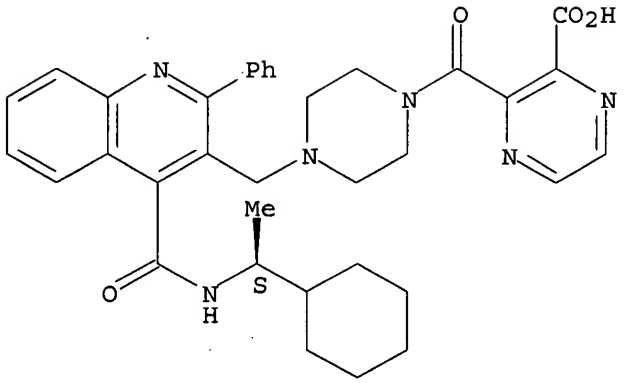
RN 425621-72-3 CAPLUS
CN 1-Piperazinepentanoic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-δ-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



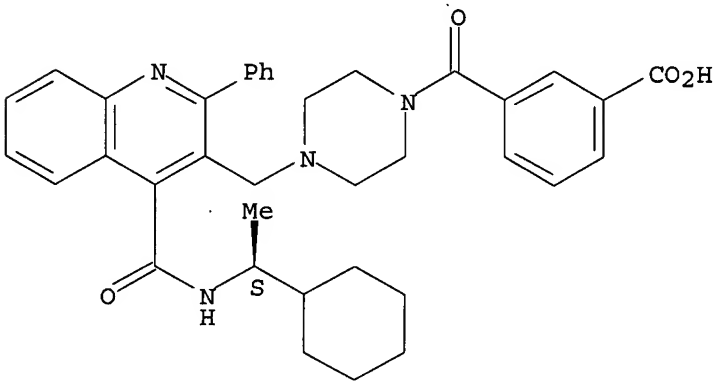
RN 425621-73-4 CAPLUS
CN Pyrazinecarboxylic acid, 3-[[4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



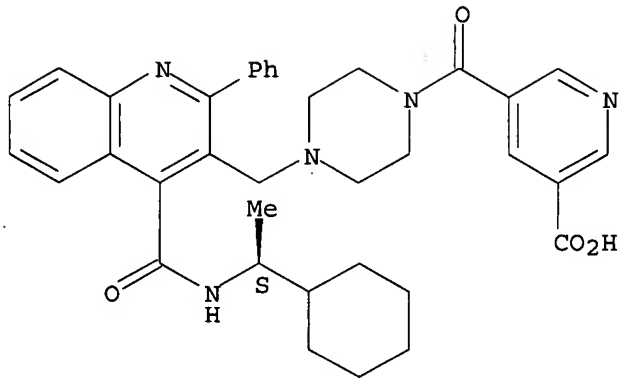
RN 425621-74-5 CAPLUS
CN Benzoic acid, 3-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



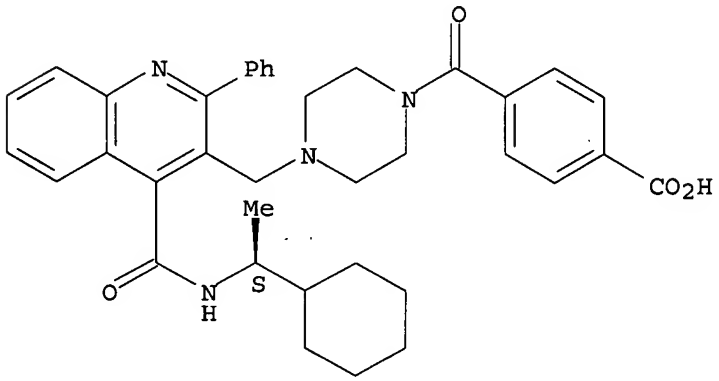
RN 425621-75-6 CAPLUS
CN 3-Pyridinecarboxylic acid, 5-[[4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



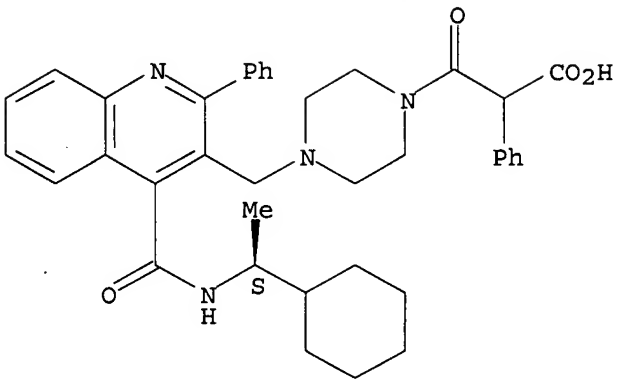
RN 425621-76-7 CAPLUS
CN Benzoic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 425621-78-9 CAPLUS
CN 1-Piperazinepropanoic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-β-oxo-α-phenyl-, monosodium salt (9CI) (CA INDEX NAME)

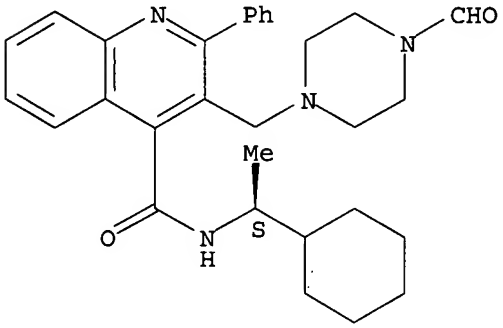
Absolute stereochemistry.



● Na

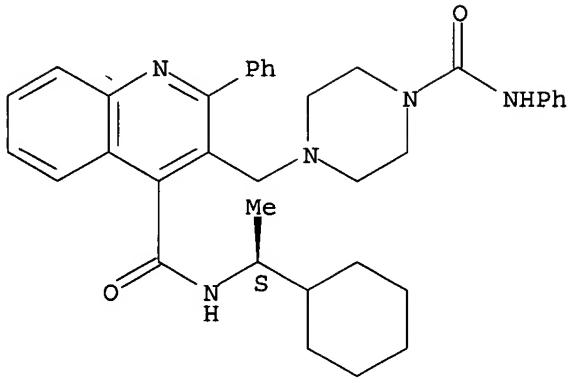
RN 425621-79-0 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[(4-formyl-1-piperazinyl)methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



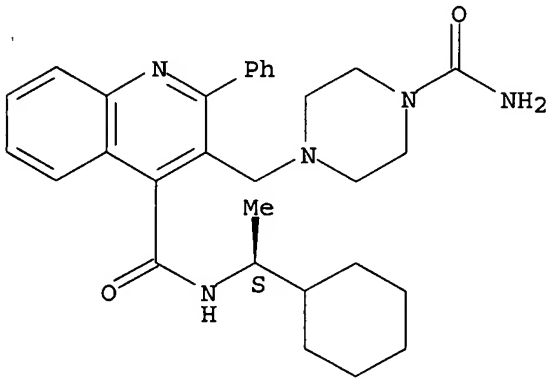
RN 425621-80-3 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-2-phenyl-3-[[4-[(phenylamino)carbonyl]-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



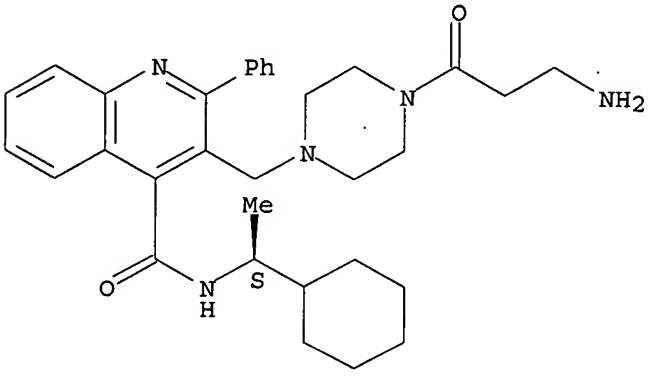
RN 425621-81-4 CAPLUS
CN 4-Quinolinecarboxamide, 3-[[4-(aminocarbonyl)-1-piperazinyl]methyl]-N-[(1S)-1-cyclohexylethyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



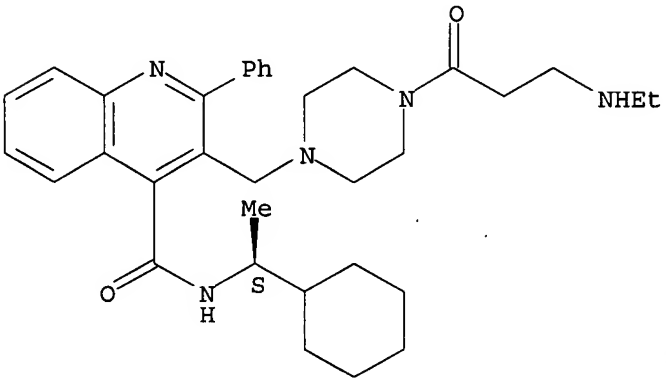
RN 425621-82-5 CAPLUS
CN 4-Quinolinecarboxamide, 3-[[4-(3-amino-1-oxopropyl)-1-piperazinyl]methyl]-N-[(1S)-1-cyclohexylethyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



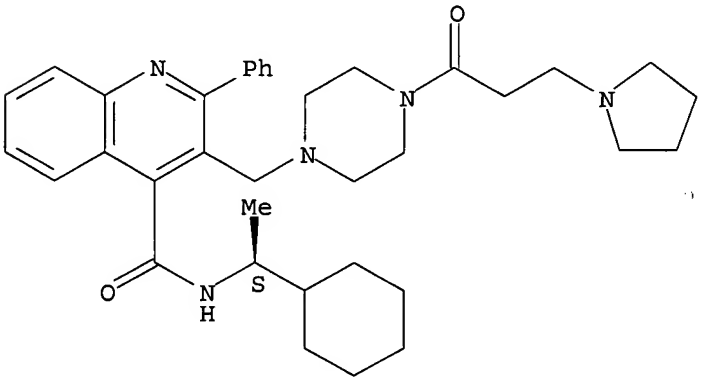
RN 425621-83-6 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-[3-(ethylamino)-1-oxopropyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



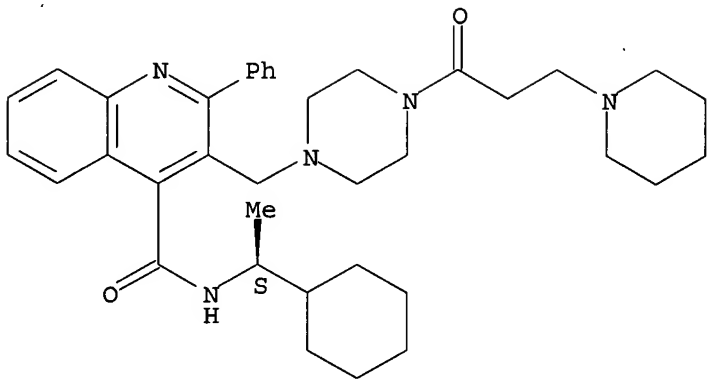
RN 425621-84-7 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-[1-oxo-3-(1-pyrrolidinyl)propyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

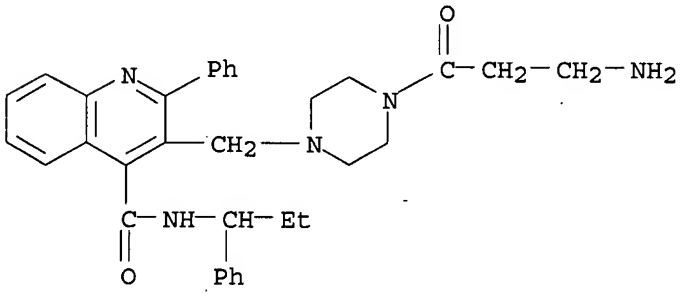


RN 425621-85-8 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-[1-oxo-3-(1-piperidinyl)propyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

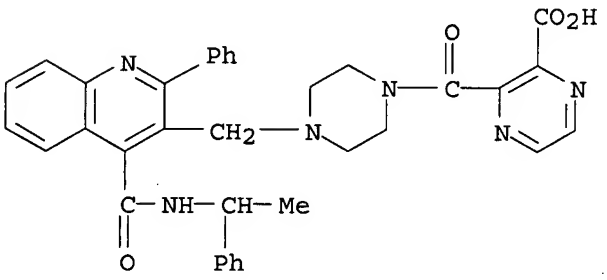
Absolute stereochemistry. Rotation (+).



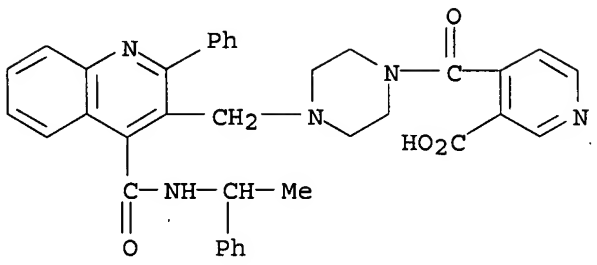
RN 425621-86-9 CAPLUS
CN 4-Quinolinecarboxamide, 3-[[4-(3-amino-1-oxopropyl)-1-piperazinyl]methyl]-2-phenyl-N-(1-phenylpropyl)- (9CI) (CA INDEX NAME)



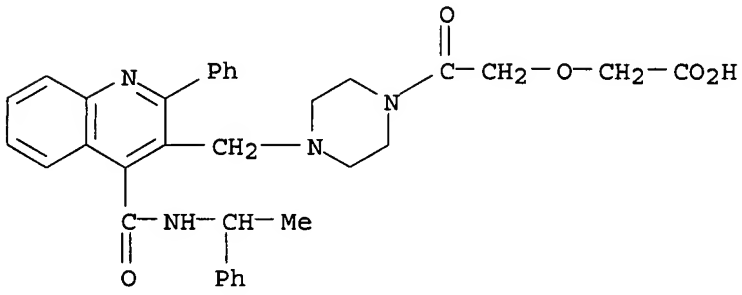
RN 425621-87-0 CAPLUS
CN Pyrazinecarboxylic acid, 3-[[4-[[2-phenyl-4-[[(1-phenylethyl)amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]-(9CI) (CA INDEX NAME)



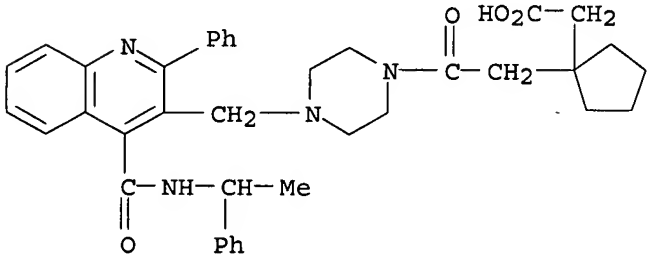
RN 425621-88-1 CAPLUS
CN 3-Pyridinecarboxylic acid, 4-[[4-[[2-phenyl-4-[[(1-phenylethyl)amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]-(9CI) (CA INDEX NAME)



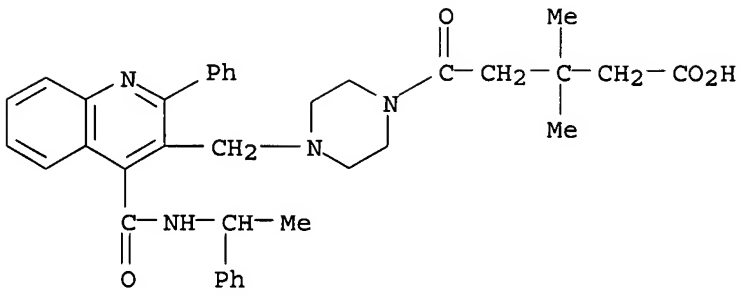
RN 425621-89-2 CAPLUS
CN Acetic acid, [2-oxo-2-[4-[[2-phenyl-4-[[(1-phenylethyl)amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]ethoxy]- (9CI) (CA INDEX NAME)



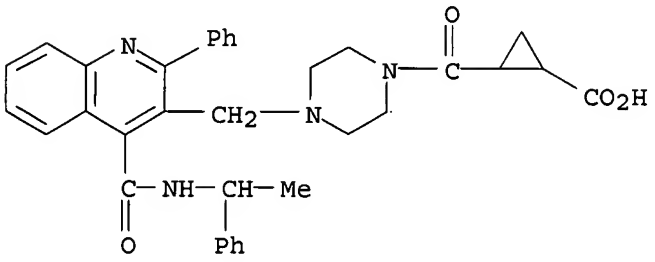
RN 425621-90-5 CAPLUS
CN Cyclopentaneacetic acid, 1-[2-oxo-2-[4-[[2-phenyl-4-[[(1-phenylethyl)amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



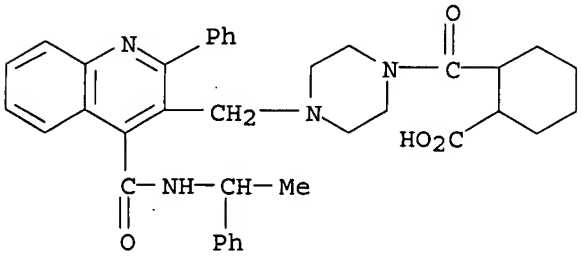
RN 425621-91-6 CAPLUS
CN 1-Piperazinepentanoic acid, β,β-dimethyl-δ-oxo-4-[[2-phenyl-4-[[(1-phenylethyl)amino]carbonyl]-3-quinolinyl]methyl]- (9CI) (CA INDEX NAME)



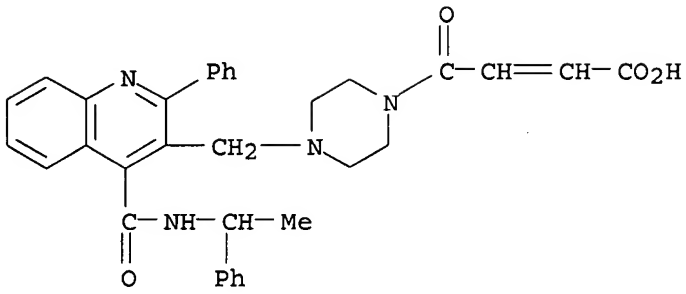
RN 425621-92-7 CAPLUS
CN Cyclopropanecarboxylic acid, 2-[[4-[[2-phenyl-4-[[(1-phenylethyl)amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)



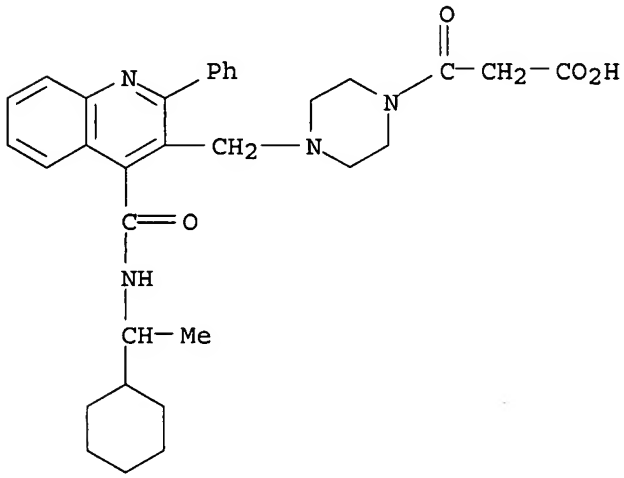
RN 425621-93-8 CAPLUS
CN Cyclohexanecarboxylic acid, 2-[[4-[[2-phenyl-4-[[(1-phenylethyl)amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)



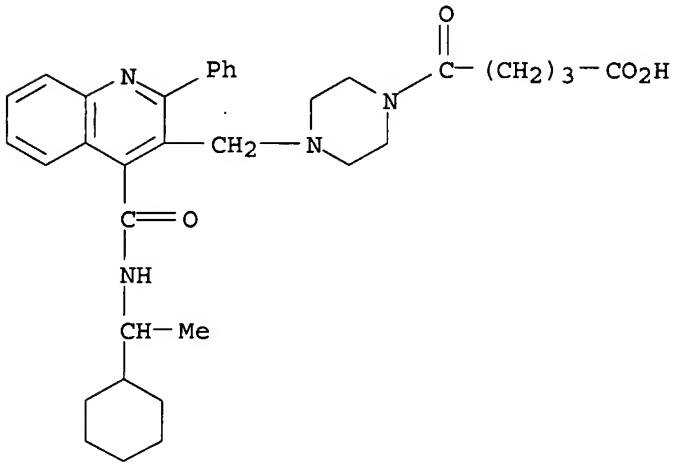
RN 425621-94-9 CAPLUS
CN 2-Butenoic acid, 4-oxo-4-[4-[[2-phenyl-4-[[(1-phenylethyl)amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



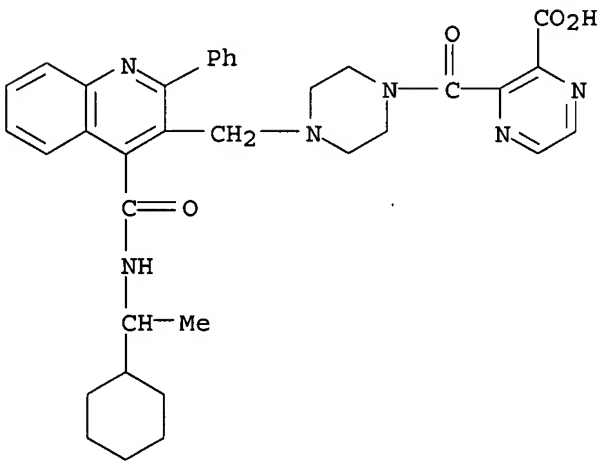
RN 425621-95-0 CAPLUS
CN 1-Piperazinepropanoic acid, 4-[[4-[[(1-cyclohexylethyl)amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-β-oxo- (9CI) (CA INDEX NAME)



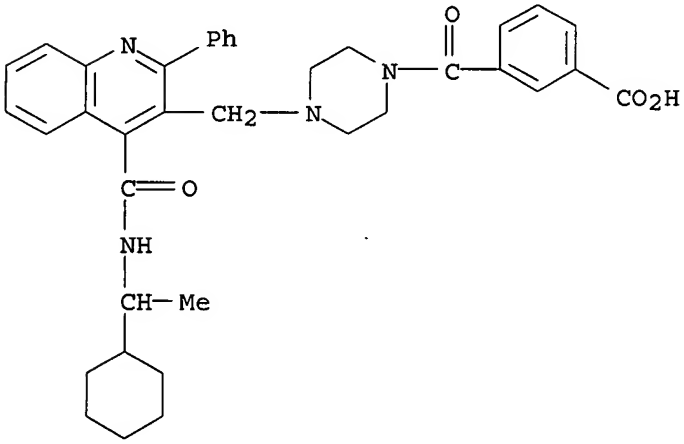
RN 425621-96-1 CAPLUS
CN 1-Piperazinepentanoic acid, 4-[[4-[[(1-cyclohexylethyl)amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-δ-oxo- (9CI) (CA INDEX NAME)



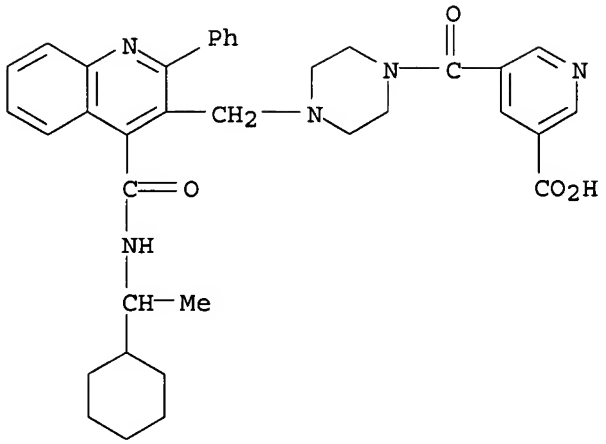
RN 425621-97-2 CAPLUS
CN Pyrazinecarboxylic acid, 3-[[4-[[4-[[(1-cyclohexylethyl)amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)



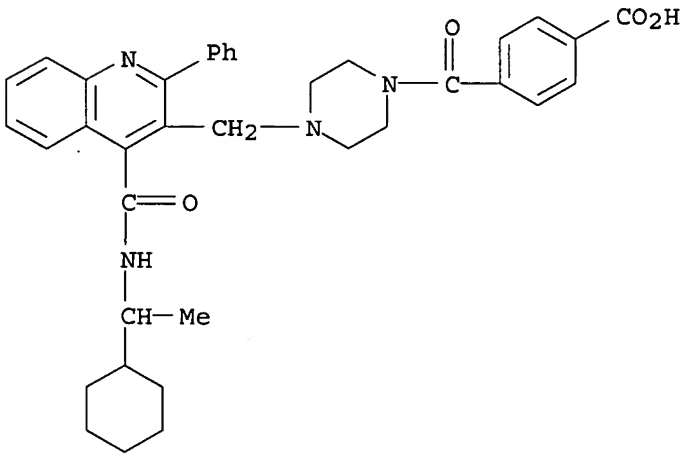
RN 425621-98-3 CAPLUS
CN Benzoic acid, 3-[[4-[[4-[[(1-cyclohexylethyl)amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)



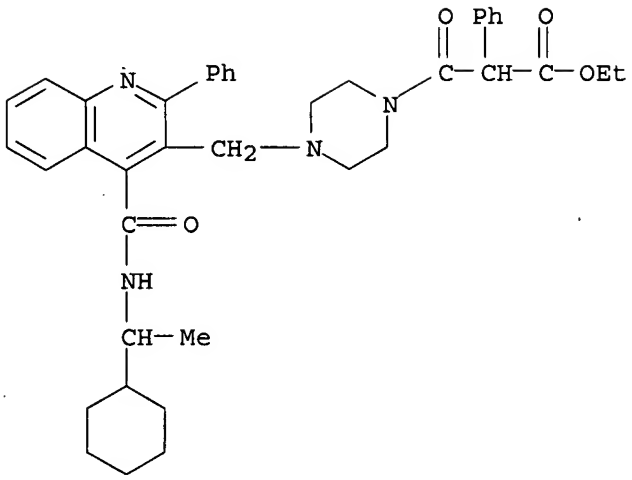
RN 425621-99-4 CAPLUS
CN 3-Pyridinecarboxylic acid, 5-[[4-[[4-[[(1-cyclohexylethyl)amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)



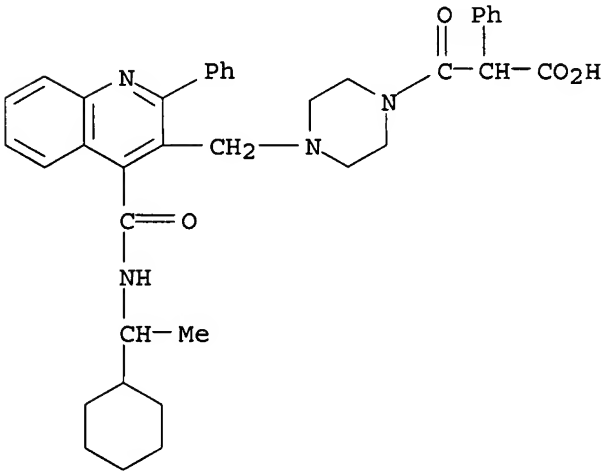
RN 425622-00-0 CAPLUS
CN Benzoic acid, 4-[[4-[[4-[[(1-cyclohexylethyl)amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)



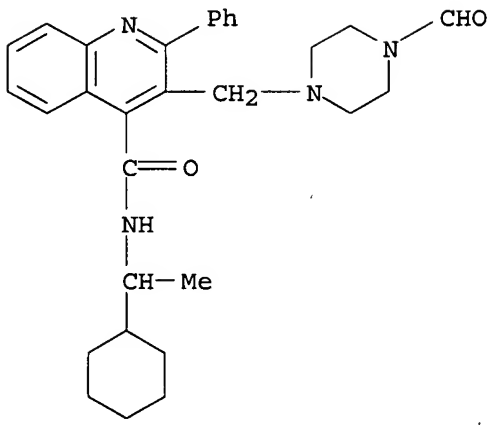
RN 425622-01-1 CAPLUS
CN 1-Piperazinepropanoic acid, 4-[[4-[[(1-cyclohexylethyl)amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-β-oxo-α-phenyl-, ethyl ester (9CI) (CA INDEX NAME)



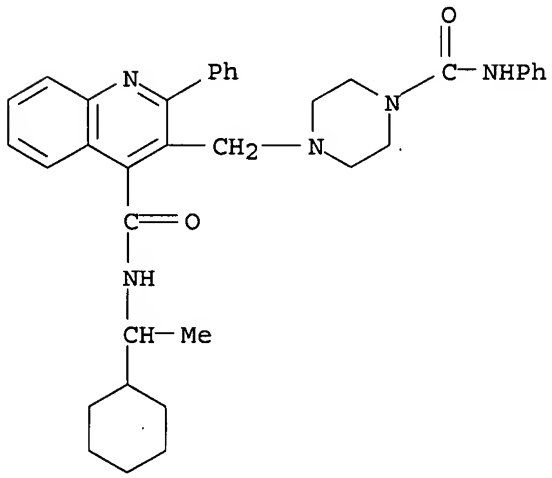
RN 425622-02-2 CAPLUS
CN 1-Piperazinepropanoic acid, 4-[[4-[[(1-cyclohexylethyl)amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-β-oxo-α-phenyl- (9CI) (CA INDEX NAME)



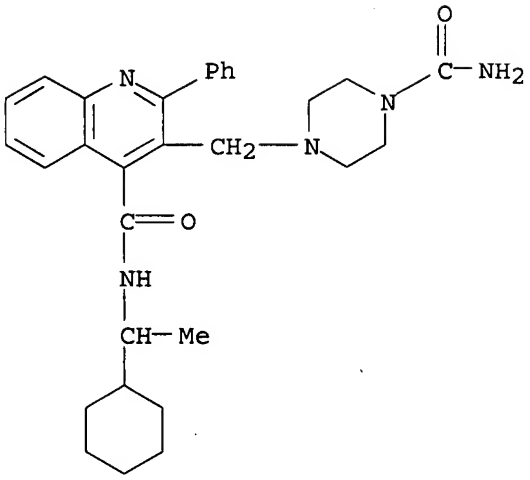
RN 425622-03-3 CAPLUS
CN 4-Quinolinecarboxamide, N-(1-cyclohexylethyl)-3-[(4-formyl-1-piperazinyl)methyl]-2-phenyl- (9CI) (CA INDEX NAME)



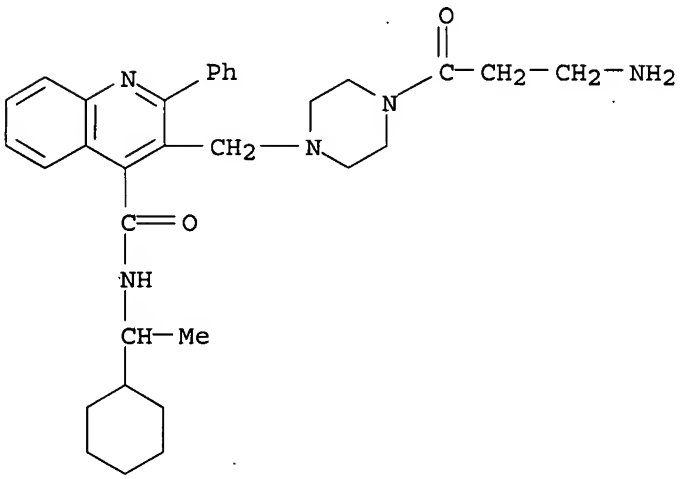
RN 425622-04-4 CAPLUS
CN 4-Quinolinecarboxamide, N-(1-cyclohexylethyl)-2-phenyl-3-[[4-[(phenylamino)carbonyl]-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



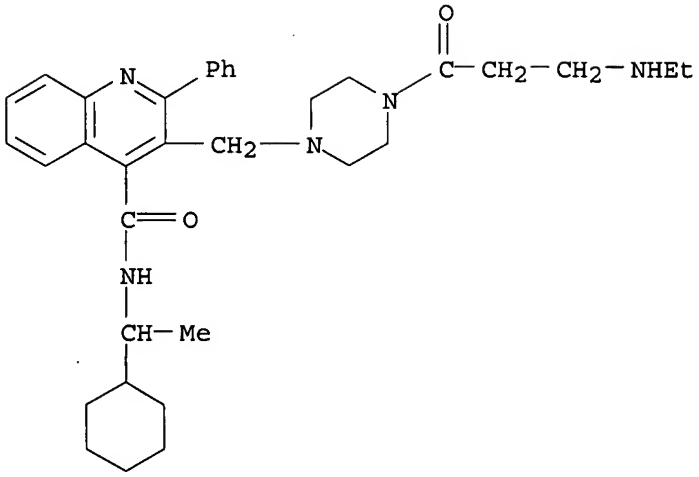
RN 425622-05-5 CAPLUS
CN 4-Quinolinecarboxamide, 3-[[4-(aminocarbonyl)-1-piperazinyl]methyl]-N-(1-cyclohexylethyl)-2-phenyl- (9CI) (CA INDEX NAME)



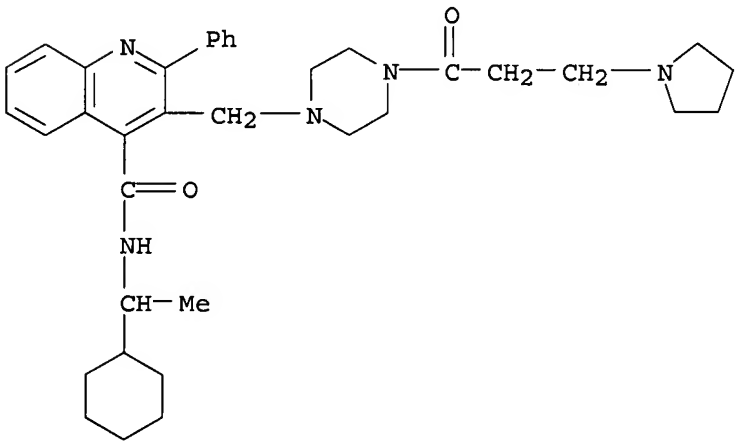
RN 425622-06-6 CAPLUS
CN 4-Quinolinecarboxamide, 3-[[4-(3-amino-1-oxopropyl)-1-piperazinyl]methyl]-N-(1-cyclohexylethyl)-2-phenyl- (9CI) (CA INDEX NAME)



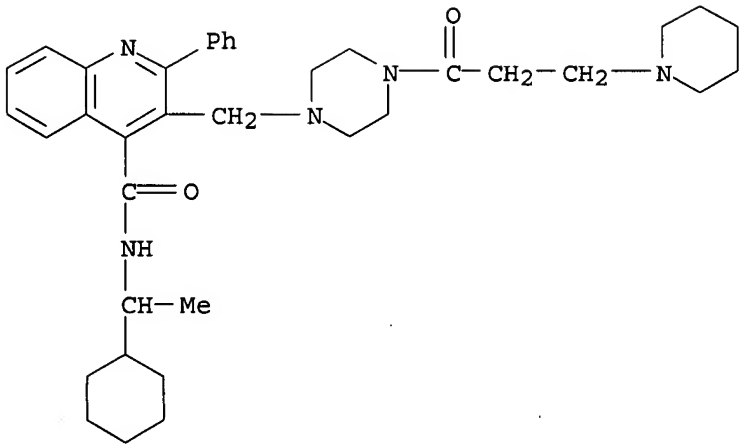
RN 425622-07-7 CAPLUS
CN 4-Quinolinecarboxamide, N-(1-cyclohexylethyl)-3-[[4-[3-(ethylamino)-1-oxopropyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)



RN 425622-08-8 CAPLUS
CN 4-Quinolinecarboxamide, N-(1-cyclohexylethyl)-3-[[4-[1-oxo-3-(1-pyrrolidinyl)propyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

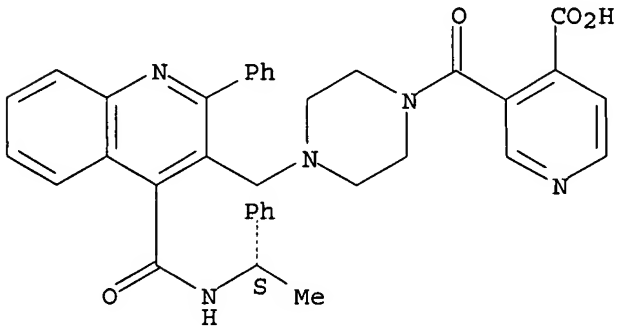


RN 425622-09-9 CAPLUS
CN 4-Quinolinecarboxamide, N-(1-cyclohexylethyl)-3-[[4-[1-oxo-3-(1-piperidinyl)propyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)



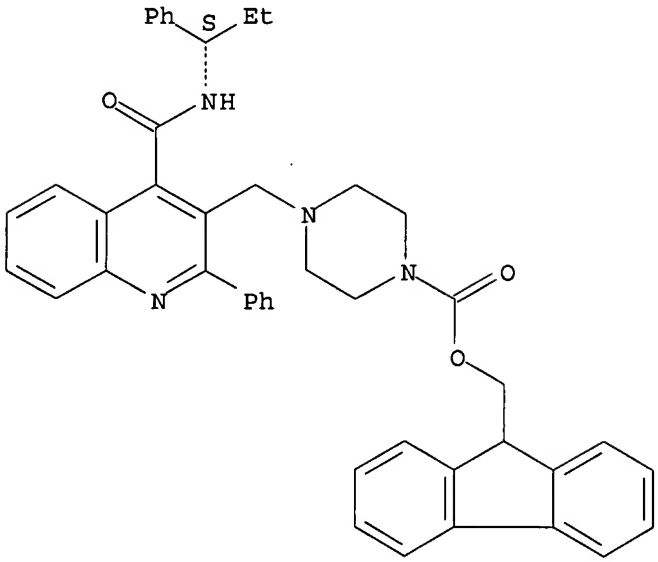
RN 425622-10-2 CAPLUS
CN 4-Pyridinecarboxylic acid, 3-[[4-[[2-phenyl-4-[[[(1S)-1-phenylethyl]amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



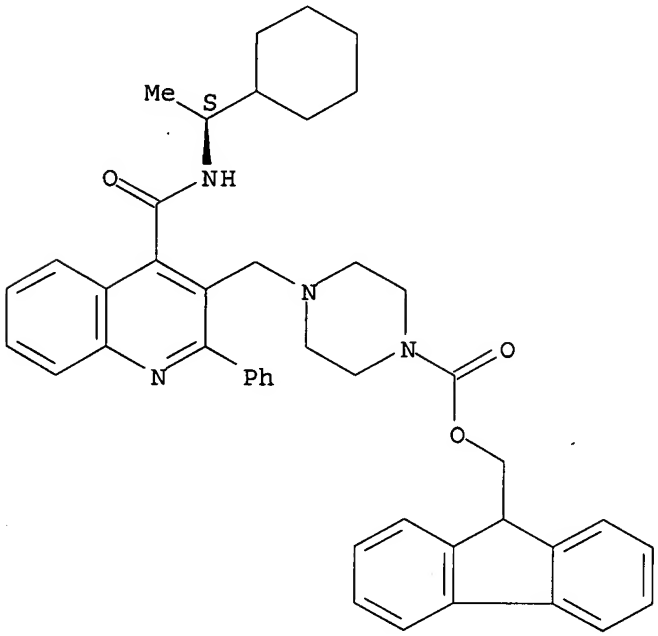
IT **270574-12-4P**, 3-[(4-Fmoc-piperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-phenylpropylamide **270574-13-5P**, 3-[(4-Fmoc-piperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-cyclohexylethylamide **425622-12-4P**, 3-[(4-Fmoc-piperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-phenylethylamide **425622-14-6P**, [3-Oxo-3-[4-[[2-phenyl-4-[((S)-1-phenylpropyl)carbamoyl]quinolin-3-yl]methyl]piperazin-1-yl]propyl]carbamic acid tert-butyl ester **425622-17-9P**, 4-[[4-[((S)-1-Cyclohexylethyl)carbamoyl]-2-phenylquinolin-3-yl]methyl]piperazine-1-carboxylic acid tert-butyl ester **425622-18-0P**, 3-[(4-Acryloylpiperazin-1-yl)methyl]-2-phenylquinoline-4-carboxylic acid (S)-1-cyclohexylethylamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of quinoline derivs. as NK-3 and NK-2 antagonists)
RN 270574-12-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[2-phenyl-4-[[[(1S)-1-phenylpropyl]amino]carbonyl]-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) . (CA INDEX NAME)

Absolute stereochemistry.



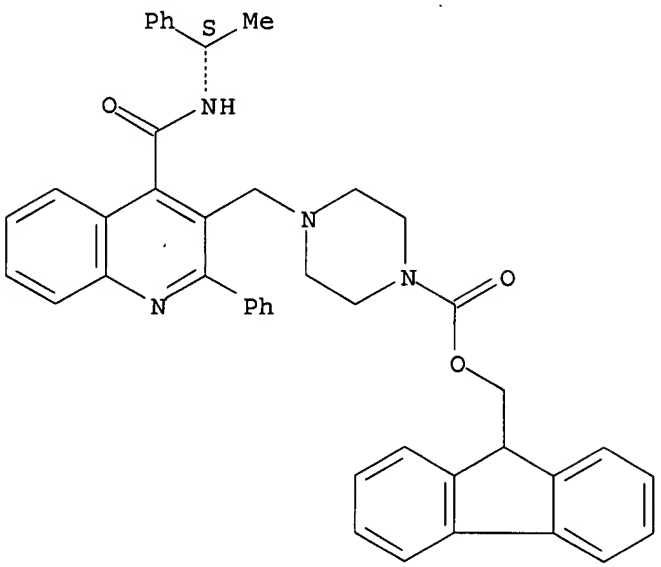
RN 270574-13-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



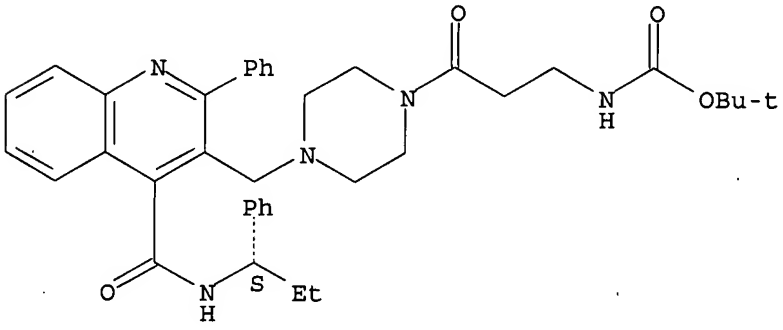
RN 425622-12-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[2-phenyl-4-[[[(1S)-1-phenylethyl]amino]carbonyl]-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



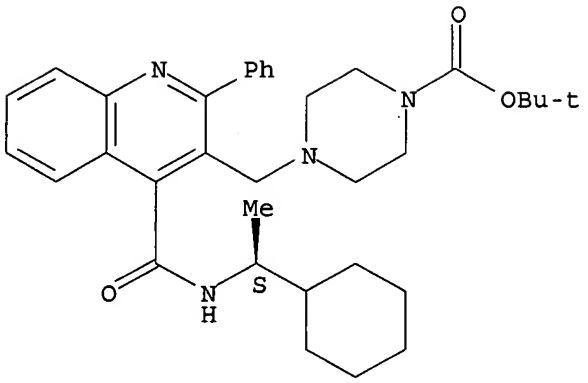
RN 425622-14-6 CAPLUS
CN Carbamic acid, [3-oxo-3-[4-[[2-phenyl-4-[[[(1S)-1-phenylpropyl]amino]carbonyl]-3-quinolinyl]methyl]-1-piperazinyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



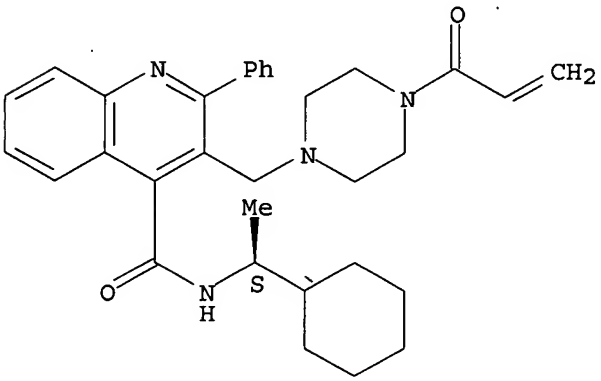
RN 425622-17-9 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 425622-18-0 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-(1-oxo-2-propenyl)-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

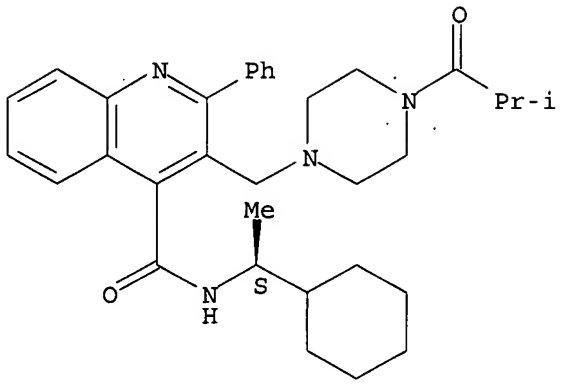
Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

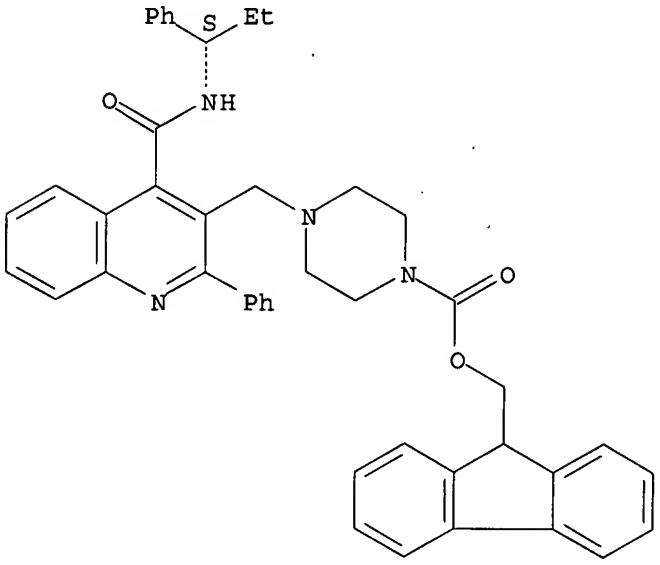
L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:290353 CAPLUS
DN 135:55462
TI Stepwise modulation of neurokinin-3 and neurokinin-2 receptor affinity and selectivity in quinoline tachykinin receptor antagonists
AU Blaney, Frank E.; Raveglia, Luca F.; Artico, Marco; Cavagnera, Stefano; Dartois, Catherine; Farina, Carlo; Grugni, Mario; Gagliardi, Stefania; Luttmann, Mark A.; Martinelli, Marisa; Nadler, Guy M. M. G.; Parini, Carlo; Petrillo, Paola; Sarau, Henry M.; Scheideler, Mark A.; Hay, Douglas W. P.; Giardina, Giuseppe A. M.
CS Department of Computational Structural Sciences, SmithKline Beecham Pharmaceuticals, Harlow Essex, CM19 5AW, UK
SO Journal of Medicinal Chemistry (2001), 44(11), 1675-1689
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB A stepwise chemical modification from human neurokinin-3 receptor (hNK-3R)-selective antagonists to potent and combined hNK-3R and hNK-2R antagonists using the same 2-phenylquinoline template is described. Docking studies with 3-D models of the hNK-3 and hNK-2 receptors were used to drive the chemical design and speed up the identification of potent and combined antagonists at both receptors. (S)-(+)-N-(1-Cyclohexylethyl)-3-[(4-morpholin-4-yl)piperidin-1-yl]methyl-2-phenylquinoline-4-carboxamide (SB-400238: hNK-3R binding affinity, Ki = 0.8 nM; hNK-2R binding affinity, Ki = 0.8 nM) emerged as the best example in this approach. Further studies led to the identification of (S)-(+)-N-(1,2,2-trimethylpropyl)-3-[(4-piperidin-1-yl)piperidin-1-yl]methyl-2-phenylquinoline-4-carboxamide (SB-414240: hNK-3R binding affinity, Ki = 193 nM; hNK-2R binding affinity, Ki = 1.0 nM) as the first hNK-2R-selective antagonist belonging to the 2-phenylquinoline chemical class. Since some members of this chemical series showed a significant binding affinity for the human μ-opioid receptor (hMOR), docking studies were also conducted on a 3-D model of the hMOR, resulting in the identification of a viable chemical strategy to avoid any significant μ-opioid component. Compds. SB-400238 and SB-414240 are therefore suitable pharmacol. tools in the tachykinin area to elucidate further the pathophysiol. role of NK-3 and NK-2 receptors and the therapeutic potential of selective NK-2 (SB-400238) or combined NK-3 and NK-2 (SB-414240) receptor antagonists.
IT **270573-24-5P 270574-12-4P 270574-13-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(stepwise modulation of neurokinin-3 and NK-2 receptor affinity and selectivity in quinoline tachykinin receptor antagonists)
RN 270573-24-5 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-(2-methyl-1-oxopropyl)-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



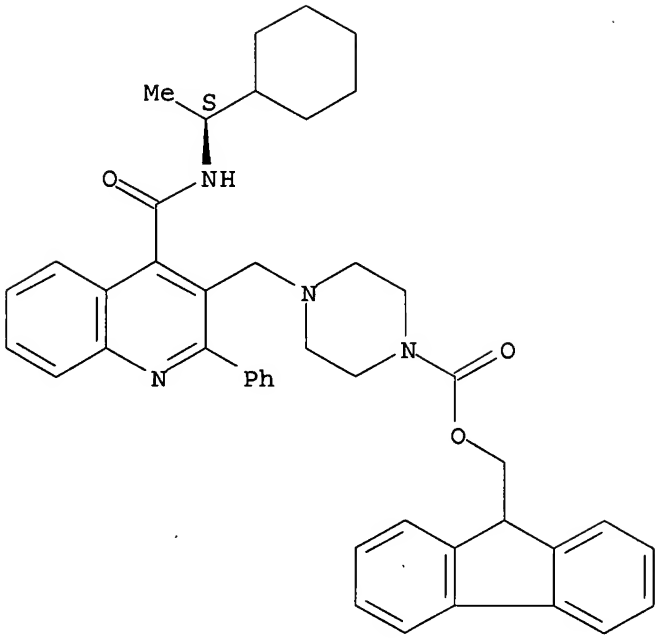
RN 270574-12-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[2-phenyl-4-[[[(1S)-1-phenylpropyl]amino]carbonyl]-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 270574-13-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:368301 CAPLUS
DN 133:4605
TI Preparation of quinoline-4-carboxamide derivatives as NK-3 and NK-2 receptor antagonists
IN Farina, Carlo; Giardina, Giuseppe; Grugni, Mario; Morvan, Marcel; Nadler, Guy Margueritte Marie Gerard; Raveglia, Luca Francesco
PA Smithkline Beecham S.P.A., Italy; Smithkline Beecham Laboratoires Pharmaceutiques
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000031037	A1	20000602	WO 1999-EP9115	19991119
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2351865	AA	20000602	CA 1999-2351865	19991119
	EP 1131295	A1	20010912	EP 1999-961001	19991119
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	TR 200101412	T2	20011022	TR 2001-200101412	19991119
	BR 9915475	A	20011218	BR 1999-15475	19991119
	NZ 511777	A	20031219	NZ 1999-511777	19991119
	AU 768708	B2	20040108	AU 2000-17770	19991119
	NO 2001002473	A	20010718	NO 2001-2473	20010518
	ZA 2001004071	A	20030107	ZA 2001-4071	20010518
	US 2003212101	A1	20031113	US 2003-358938	20030205
	US 6780875	B2	20040824		
PRAI	GB 1998-25552	A	19981120		
	GB 1998-25553	A	19981120		
	WO 1999-EP9115	W	19991119		
	US 2001-856085	B1	20010904		
	US 2002-159218	B1	20020531		

OS MARPAT 133:4605
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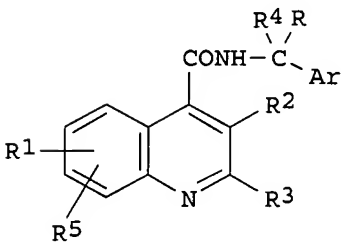


I

AB The title compds. of formula I [Ar = optionally substituted aryl or a C5-7

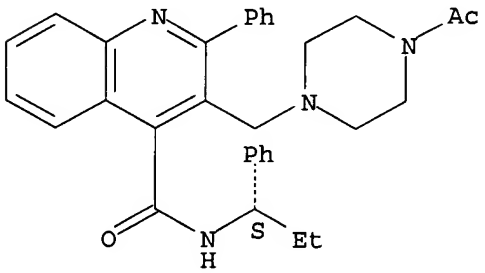
cycloalkdienyl group, or an optionally substituted C5-7 cycloalkyl group, or an optionally substituted single or fused ring aromatic heterocyclic group; R = H, linear or branched C1-6 alkyl, C3-7 cycloalkyl, C3-7 cycloalkylalkyl, R1 = H or up to three optional substituents selected from the list consisting of: C1-6 alkyl, C1-6 alkenyl, aryl, C1-6 alkoxy, OH, halogen, NO2, CN, etc; R2 = (CH2)nNY1Y2; n = an integer ranging from 1 - 9; Y1, Y2 independently = (un)substituted C1-6 alkyl or together with N to which they are attached represent optionally substituted N linked single or fused ring heterocyclic group; R3 = branched or linear C1-6 alkyl, C3-7 cycloalkyl, C4-7 cycloalkyl, etc; R4 = H, C1-6 alkyl; R5 = H, halogen] useful as NK-3 and NK-2 receptor antagonists (no data given) are prepared

IT **270573-22-3P 270573-23-4P 270573-24-5P**
270573-31-4P 270573-47-2P 270573-48-3P
270573-49-4P 270573-52-9P 270573-53-0P
270573-84-7P 270573-88-1P 270573-91-6P
270573-92-7P 270573-93-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinoline-4-carboxamide derivs. as NK-3 and NK-2 receptor antagonists)

RN 270573-22-3 CAPLUS

CN 4-Quinolinecarboxamide, 3-[(4-acetyl-1-piperazinyl)methyl]-2-phenyl-N-[(1S)-1-phenylpropyl]- (9CI) (CA INDEX NAME)

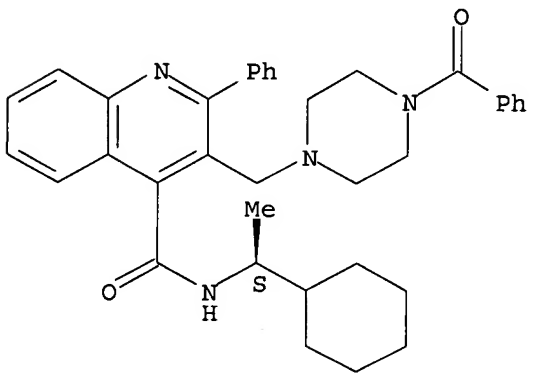
Absolute stereochemistry.



RN 270573-23-4 CAPLUS

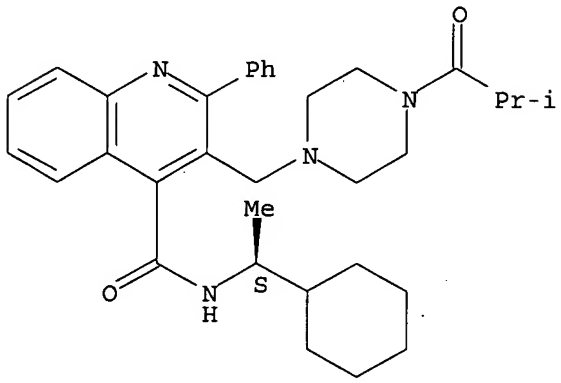
CN 4-Quinolinecarboxamide, 3-[(4-benzoyl-1-piperazinyl)methyl]-N-[(1S)-1-cyclohexylethyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



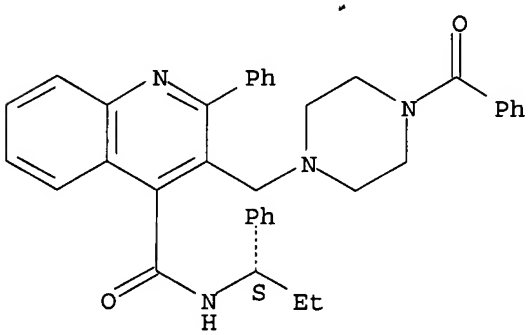
RN 270573-24-5 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-(2-methyl-1-oxopropyl)-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 270573-31-4 CAPLUS
CN 4-Quinolinecarboxamide, 3-[(4-benzoyl-1-piperazinyl)methyl]-2-phenyl-N-[(1S)-1-phenylpropyl]-, hydrochloride (2:3) (9CI) (CA INDEX NAME)

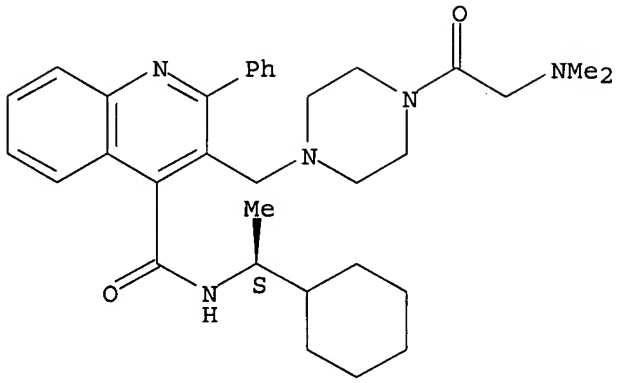
Absolute stereochemistry.



●3/2 HCl

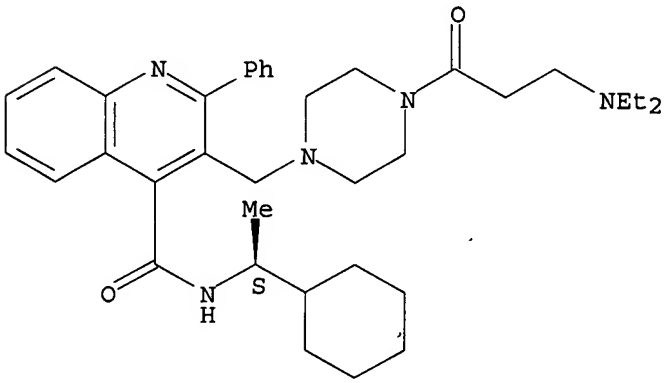
RN 270573-47-2 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-[(dimethylamino)acetyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



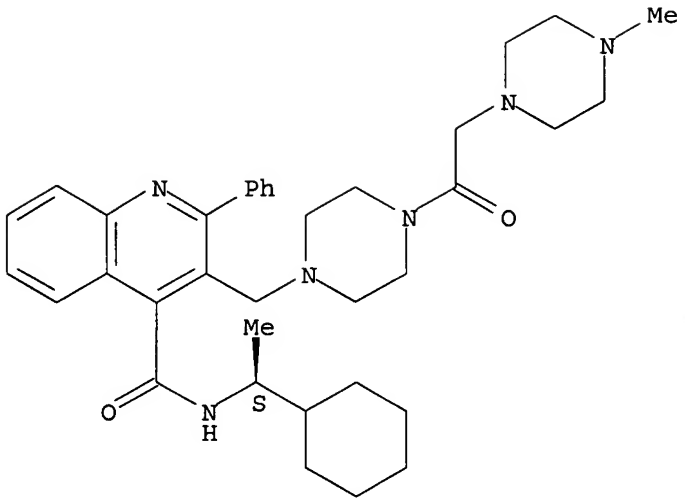
RN 270573-48-3 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-[3-(diethylamino)-1-oxopropyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



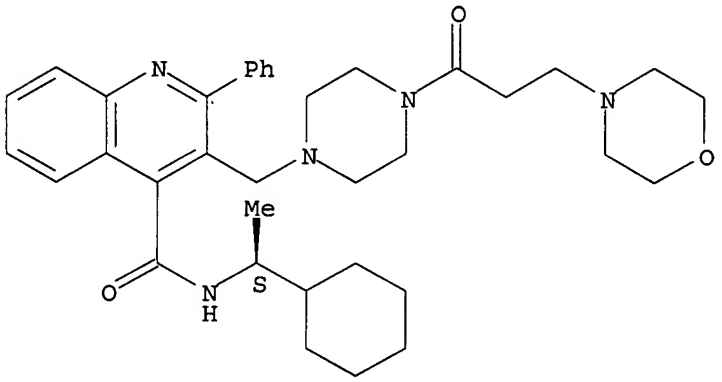
RN 270573-49-4 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-[(4-methyl-1-piperazinyl)acetyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



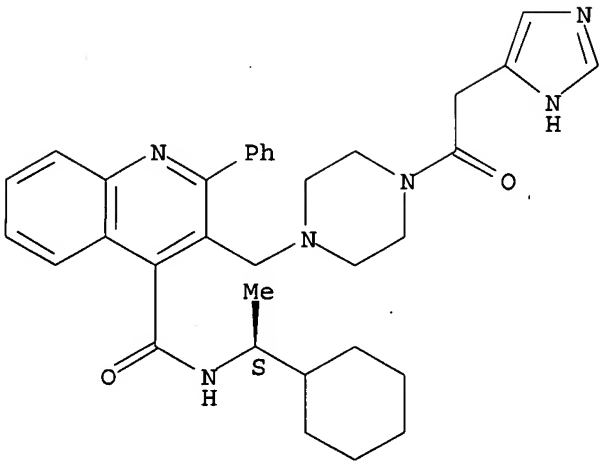
RN 270573-52-9 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-[3-(4-morpholinyl)-1-oxopropyl]-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



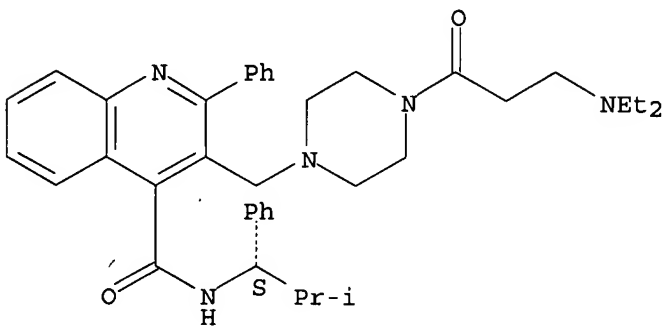
RN 270573-53-0 CAPLUS
CN 4-Quinolinecarboxamide, N-[(1S)-1-cyclohexylethyl]-3-[[4-(1H-imidazol-4-ylacetyl)-1-piperazinyl]methyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



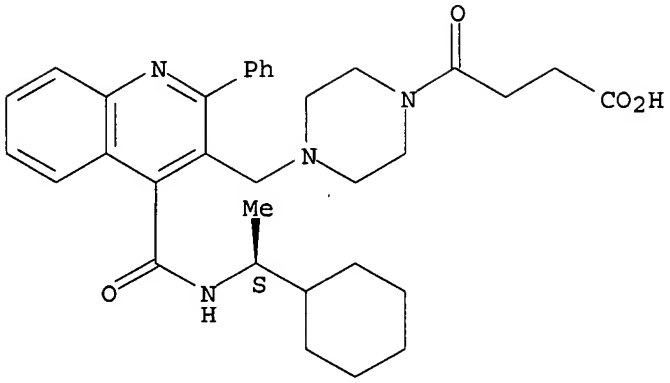
RN 270573-84-7 CAPLUS
CN 4-Quinolinecarboxamide, 3-[[4-[3-(diethylamino)-1-oxopropyl]-1-piperazinyl]methyl]-N-[(1S)-2-methyl-1-phenylpropyl]-2-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



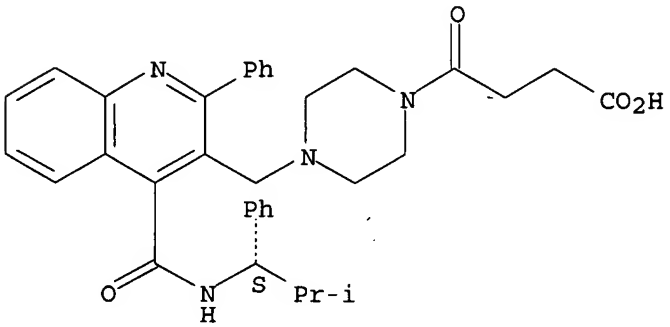
RN 270573-88-1 CAPLUS
CN 1-Piperazinebutanoic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-γ-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



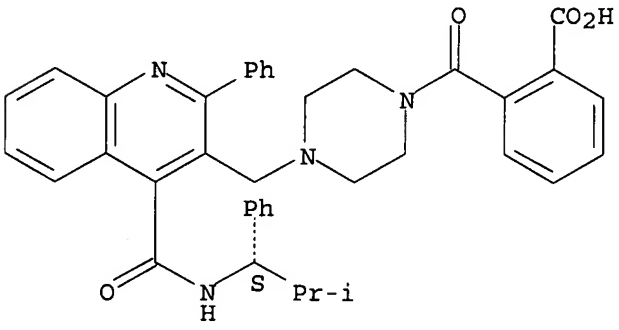
RN 270573-91-6 CAPLUS
CN 1-Piperazinebutanoic acid, 4-[[4-[[[(1S)-2-methyl-1-phenylpropyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-γ-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 270573-92-7 CAPLUS
CN Benzoic acid, 2-[[4-[[4-[[[(1S)-2-methyl-1-phenylpropyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)

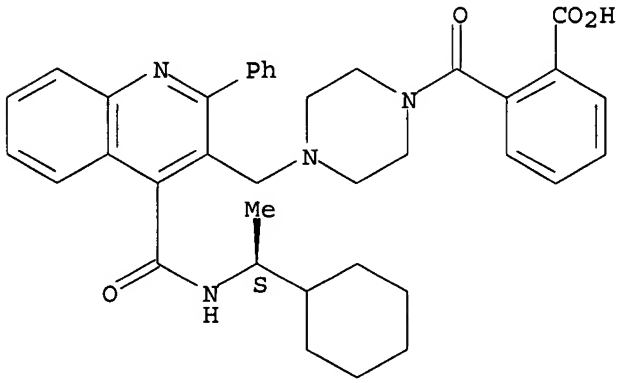
Absolute stereochemistry.



RN 270573-93-8 CAPLUS

CN Benzoic acid, 2-[[4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)

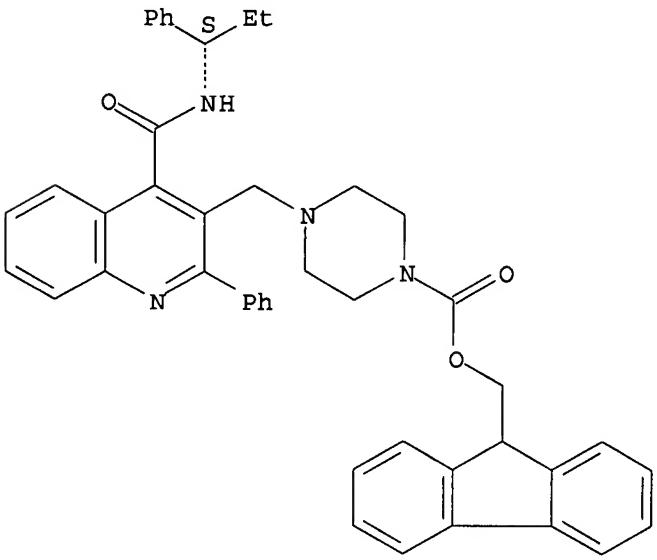
Absolute stereochemistry.



IT **270574-12-4P 270574-13-5P 270574-14-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinoline-4-carboxamide derivs. as NK-3 and NK-2 receptor antagonists)

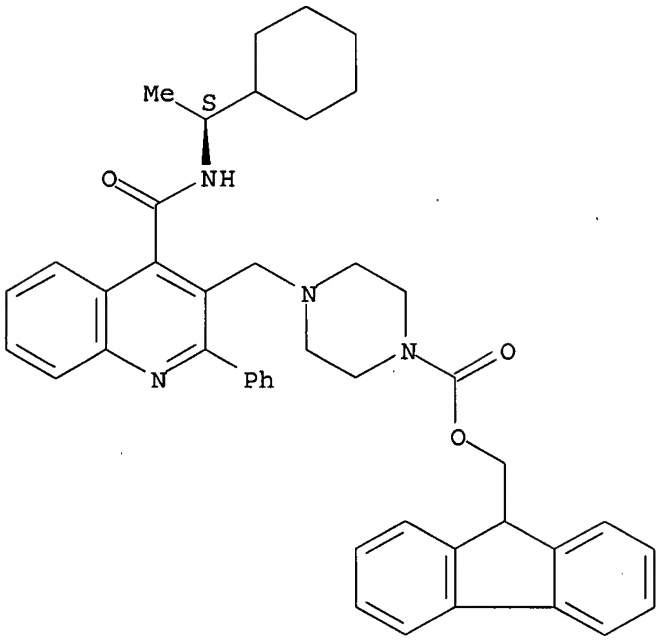
RN 270574-12-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[2-phenyl-4-[[[(1S)-1-phenylpropyl]amino]carbonyl]-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



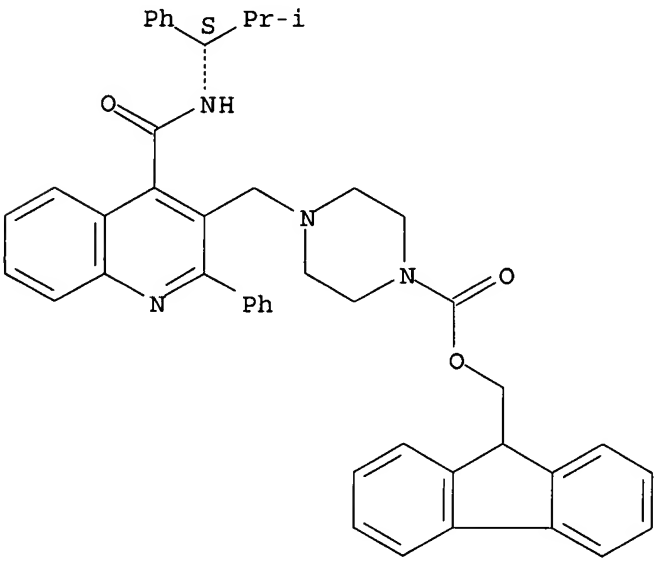
RN 270574-13-5 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-1-cyclohexylethyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 270574-14-6 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[[4-[[[(1S)-2-methyl-1-phenylpropyl]amino]carbonyl]-2-phenyl-3-quinolinyl]methyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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